10/275,899

Mohamed ~~RCT/US01/05~~825

=> d his

(FILE 'HCAPLUS' ENTERED AT 08:45:44 ON 09 JUL 2001)
DEL HIS Y

FILE 'REGISTRY' ENTERED AT 08:46:11 ON 09 JUL 2001
ACT MOHAMED/A

L1 (700)SEA FILE=REGISTRY ABB=ON G[RG][VLG][CL]VQ[PD]G/SQSP
L2 24 SEA FILE=REGISTRY ABB=ON L1 AND SQL=8

FILE 'HCAPLUS' ENTERED AT 08:46:20 ON 09 JUL 2001
L3 2 S L2
L4 8 S ZONULIN#
L5 8 S ZONULIN#/AB
L6 8 S L4 OR L5
L7 37 S ZONULA OCCLUDENS (L) TOXIN#
L8 7 S L7 (L) RECEPTOR#
L9 3 S L8 NOT L6

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 08:47:42 ON 09 JUL 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:    8 JUL 2001  HIGHEST RN 344899-57-6
DICTIONARY FILE UPDATES:   8 JUL 2001  HIGHEST RN 344899-57-6

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.

=> d que stat l2

L1    (      700)SEA FILE=REGISTRY ABB=ON  G[RG][VLG][CL]VQ[PD]G/SQSP
L2            24 SEA FILE=REGISTRY ABB=ON  L1 AND SQL=8
```

SEQ. search

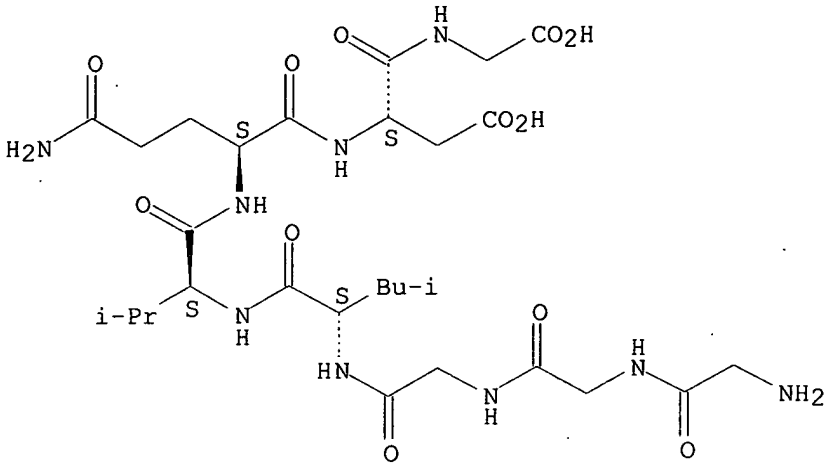
```
=> d l2 sqide3 1-24

L2   ANSWER 1 OF 24  REGISTRY  COPYRIGHT 2001 ACS
RN   258818-43-8  REGISTRY
CN   Glycine, glycylglycylglycyl-L-leucyl-L-valyl-L-glutaminyl-L-.alpha.-
     aspartyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   24: PN: WO0007609 SEQID: 24 claimed sequence
FS   PROTEIN SEQUENCE; STEREOSEARCH
SQL  8

SEQ3      1 Gly-Gly-Gly-Leu-Val-Gln-Asp-Gly
            === === === === === === === ===
HITS AT:    1-8

MF   C28 H47 N9 O12
SR   CA
LC   STN Files:   CA, CAPLUS, TOXLIT

Absolute stereochemistry.
```



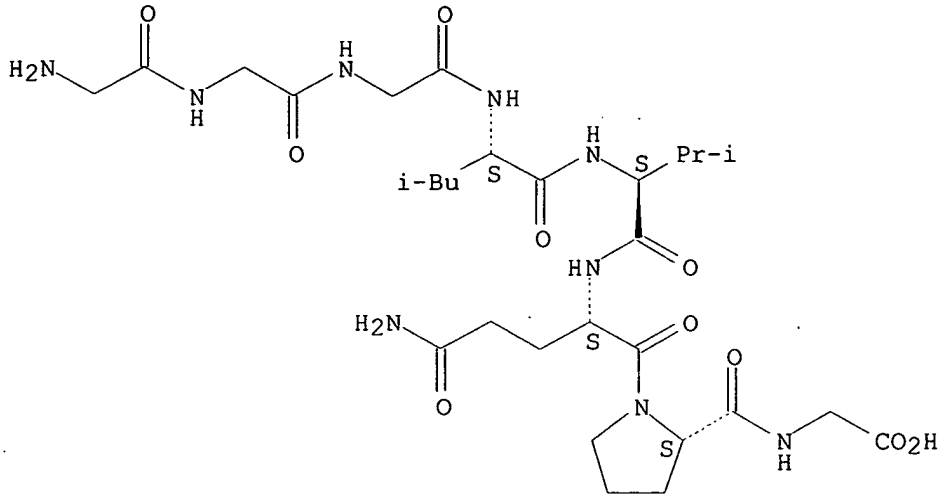
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 2 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-42-7 REGISTRY
CN Glycine, glycylglycylglycyl-L-leucyl-L-valyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 23: PN: WO0007609 SEQID: 23 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 8

SEQ3 1 Gly-Gly-Gly-Leu-Val-Gln-Pro-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C29 H49 N9 O10
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



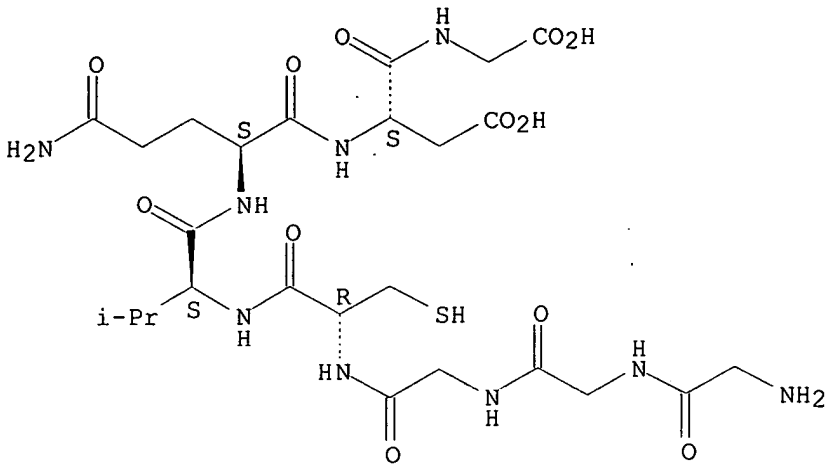
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 3 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-41-6 REGISTRY
CN Glycine, glycylglycylglycyl-L-cysteinyl-L-valyl-L-glutaminyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 22: PN: WO0007609 SEQID: 22 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Gly-Gly-Cys-Val-Gln-Asp-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C25 H41 N9 O12 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



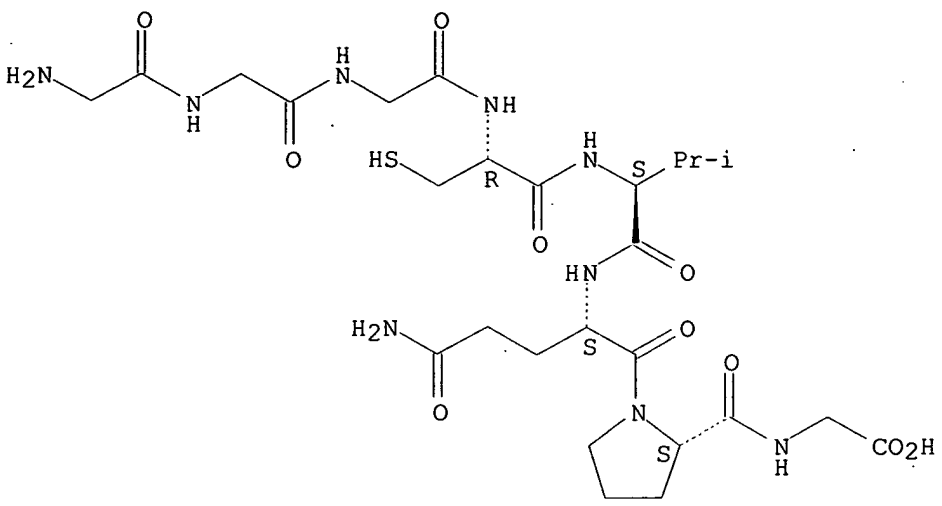
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 4 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-40-5 REGISTRY
CN Glycine, glycylglycylglycyl-L-cysteinyl-L-valyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 21: PN: WO0007609 SEQID: 21 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 8

SEQ3 1 Gly-Gly-Gly-Cys-Val-Gln-Pro-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C26 H43 N9 O10 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

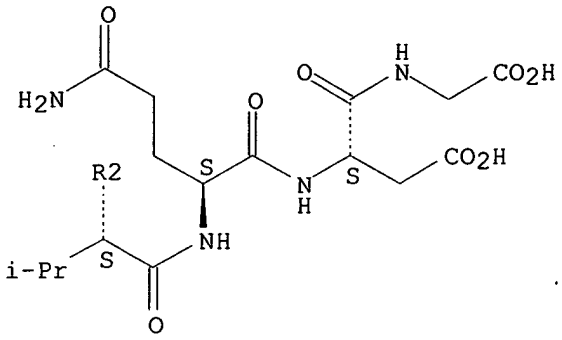
L2 ANSWER 5 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-39-2 REGISTRY
CN Glycine, glycylglycyl-L-leucyl-L-leucyl-L-valyl-L-glutaminyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 20: PN: WO0007609 SEQID: 20 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Gly-Leu-Leu-Val-Gln-Asp-Gly
=== === === === === === === ===
HITS AT: 1-8

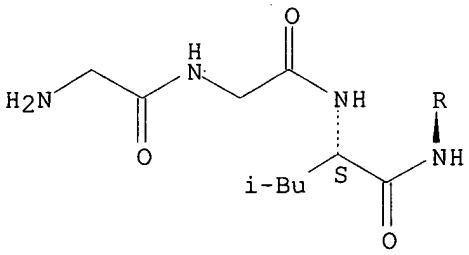
MF C32 H55 N9 O12
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

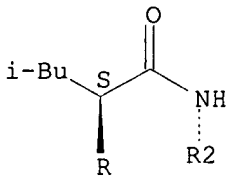
Absolute stereochemistry.

PAGE 1-A



PAGE 2-A





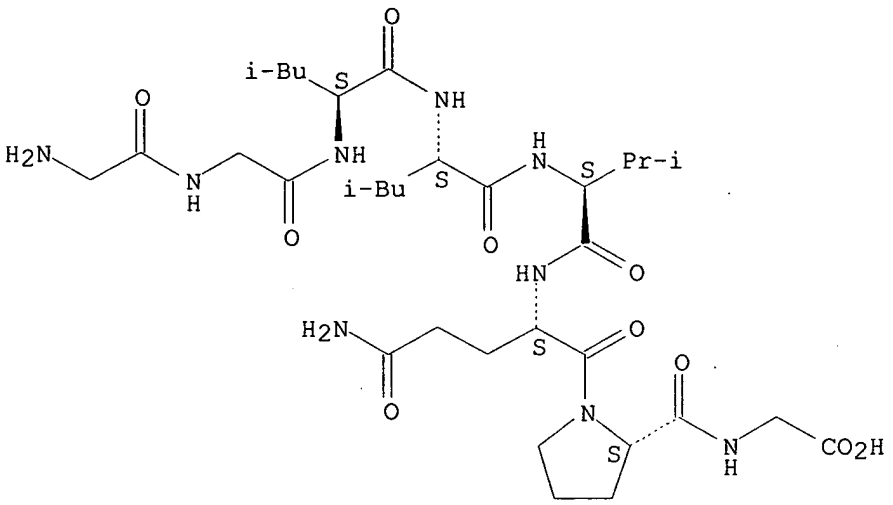
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 6 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-38-1 REGISTRY
CN Glycine, glycylglycyl-L-leucyl-L-leucyl-L-valyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 19: PN: WO0007609 SEQID: 19 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Gly-Leu-Leu-Val-Gln-Pro-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C33 H57 N9 O10
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



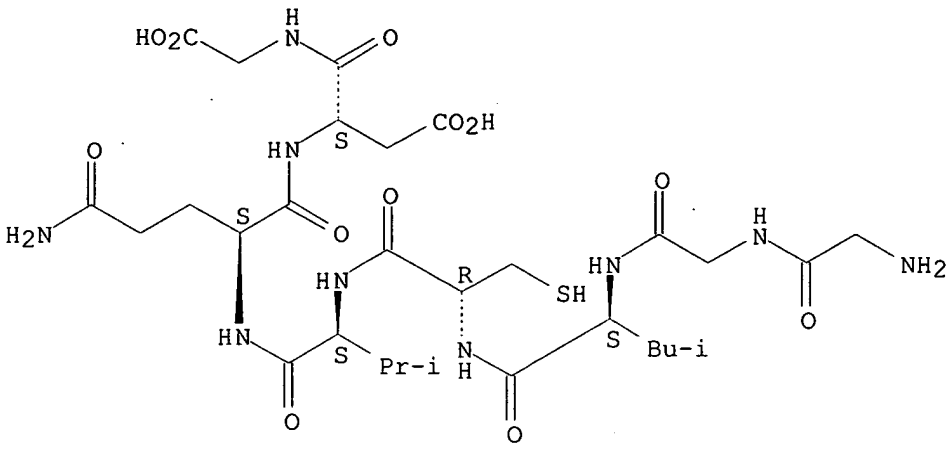
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 7 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-37-0 REGISTRY
CN Glycine,
glycylglycyl-L-leucyl-L-cysteinyl-L-valyl-L-glutaminyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 18: PN: WO0007609 SEQID: 18 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 8

SEQ3 1 Gly-Gly-Leu-Cys-Val-Gln-Asp-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C29 H49 N9 O12 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



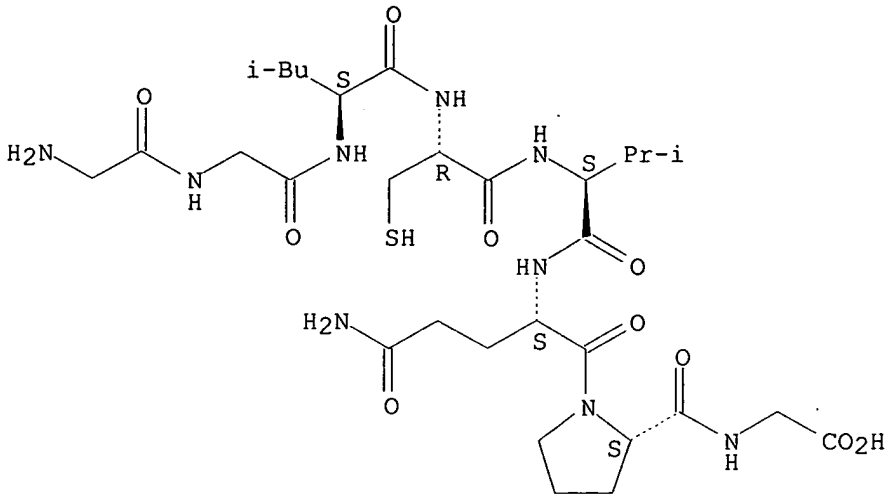
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 8 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-36-9 REGISTRY
CN Glycine, glycylglycyl-L-leucyl-L-cysteinyl-L-valyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 17: PN: WO0007609 SEQID: 17 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Gly-Leu-Cys-Val-Gln-Pro-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C30 H51 N9 O10 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

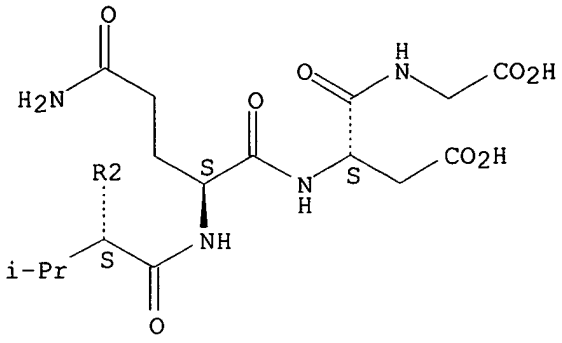
L2 ANSWER 9 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-35-8 REGISTRY
CN Glycine, glycylglycyl-L-valyl-L-leucyl-L-valyl-L-glutaminyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 16: PN: WO0007609 SEQID: 16 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Gly-Val-Leu-Val-Gln-Asp-Gly
=== === === === === === === ===
HITS AT: 1-8

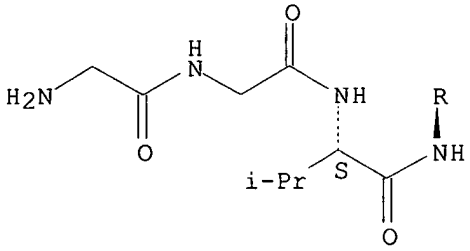
MF C31 H53 N9 O12
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

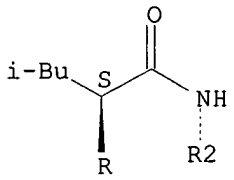
Absolute stereochemistry.

PAGE 1-A



PAGE 2-A





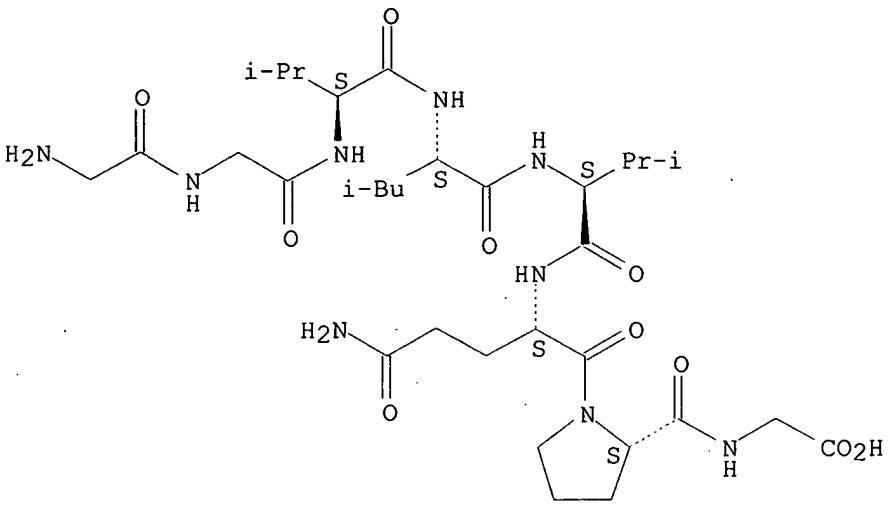
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 10 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-34-7 REGISTRY
CN Glycine, glycylglycyl-L-valyl-L-leucyl-L-valyl-L-glutaminyl-L-prolyl-
(9CI) (CA INDEX NAME)
OTHER NAMES:
CN 15: PN: WO0007609 SEQID: 15 claimed sequence
CN 1: PN: WO0015252 SEQID: 7 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Gly-Val-Leu-Val-Gln-Pro-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C32 H55 N9 O10
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



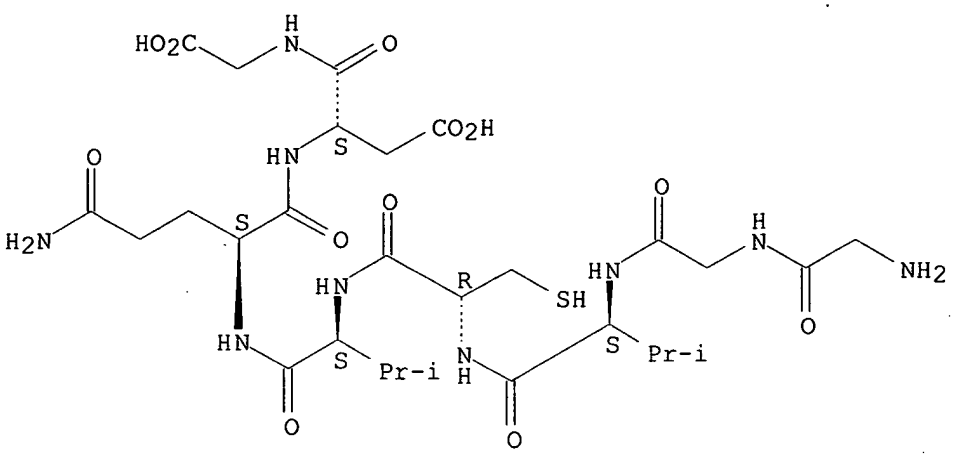
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 11 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-33-6 REGISTRY
CN Glycine, glycylglycyl-L-valyl-L-cysteinyl-L-valyl-L-glutaminyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 14: PN: WO0007609 SEQID: 14 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Gly-Val-Cys-Val-Gln-Asp-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C28 H47 N9 O12 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



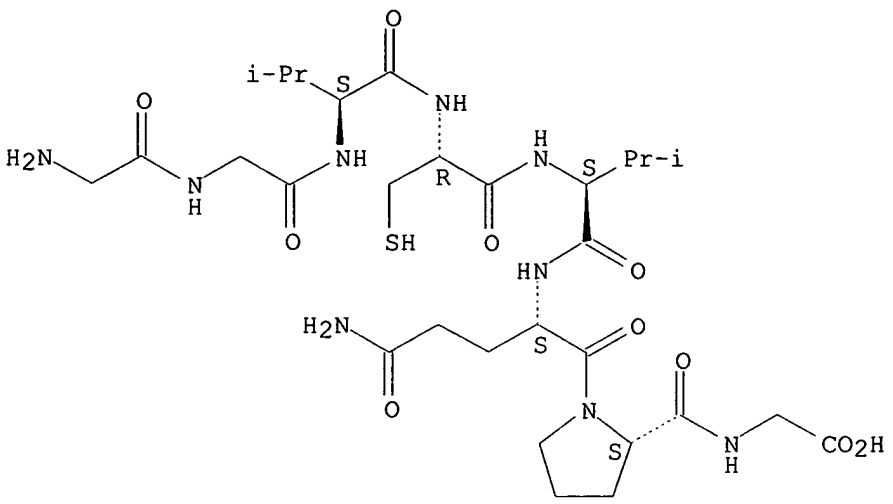
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 12 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-32-5 REGISTRY
CN Glycine, glycylglycyl-L-valyl-L-cysteinyl-L-valyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 13: PN: WO0007609 SEQID: 13 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Gly-Val-Cys-Val-Gln-Pro-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C29 H49 N9 O10 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



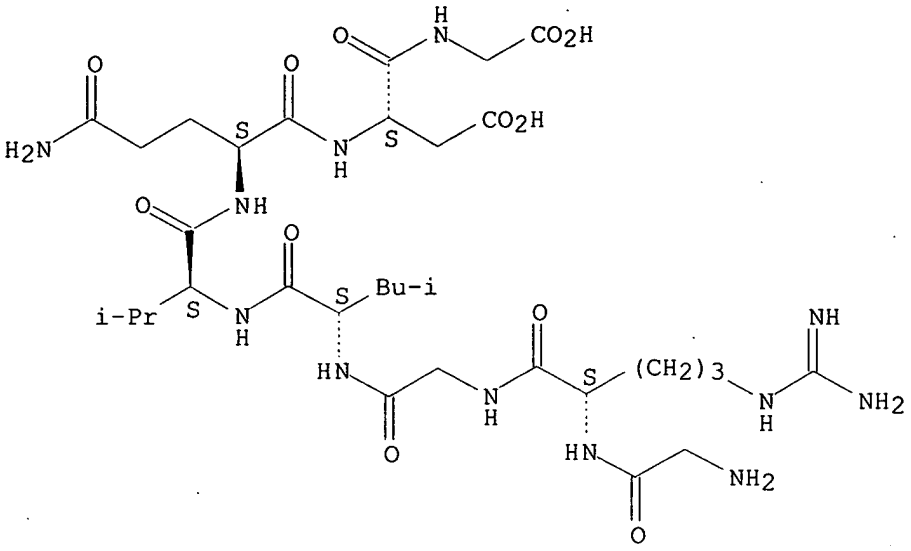
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 13 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-31-4 REGISTRY
CN Glycine, glycyl-L-arginylglycyl-L-leucyl-L-valyl-L-glutaminyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 12: PN: WO0007609 SEQID: 12 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 8

SEQ3 1 Gly-Arg-Gly-Leu-Val-Gln-Asp-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C32 H56 N12 O12
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



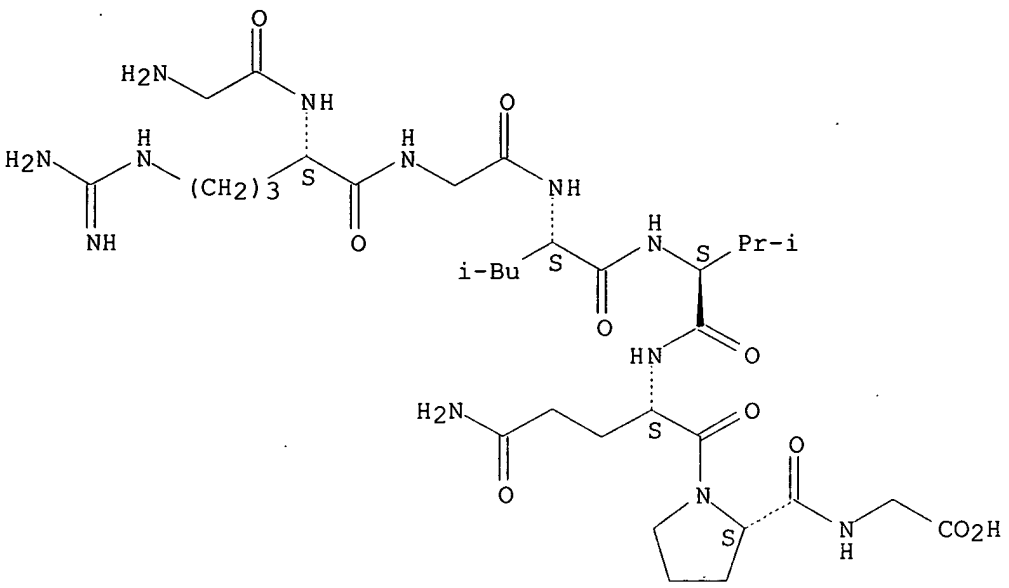
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 14 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-30-3 REGISTRY
CN Glycine, glycyl-L-arginylglycyl-L-leucyl-L-valyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 11: PN: WO0007609 SEQID: 11 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Arg-Gly-Leu-Val-Gln-Pro-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C33 H58 N12 O10
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



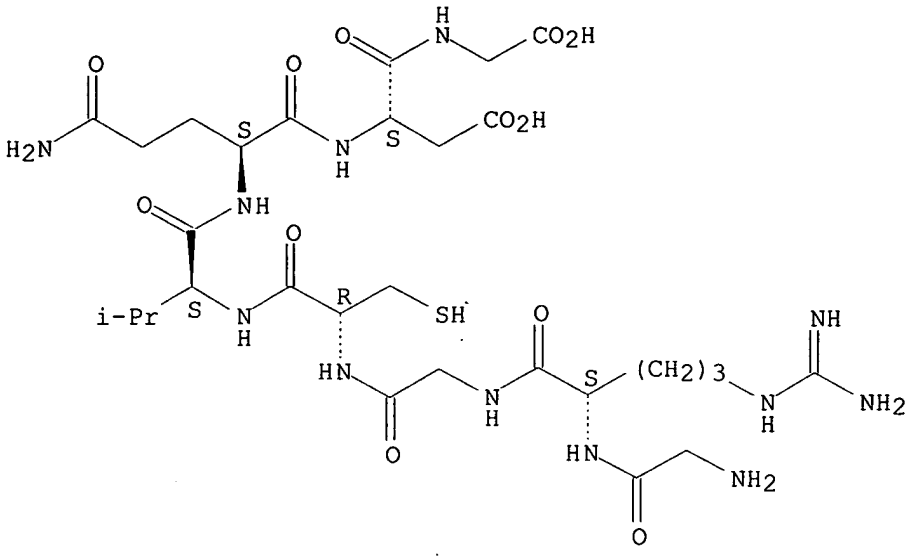
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 15 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-29-0 REGISTRY
CN Glycine,
glycyl-L-arginylglycyl-L-cysteinyl-L-valyl-L-glutaminyl-L-.alpha.-
aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 10: PN: WO0007609 SEQID: 10 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Arg-Gly-Cys-Val-Gln-Asp-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C29 H50 N12 O12 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



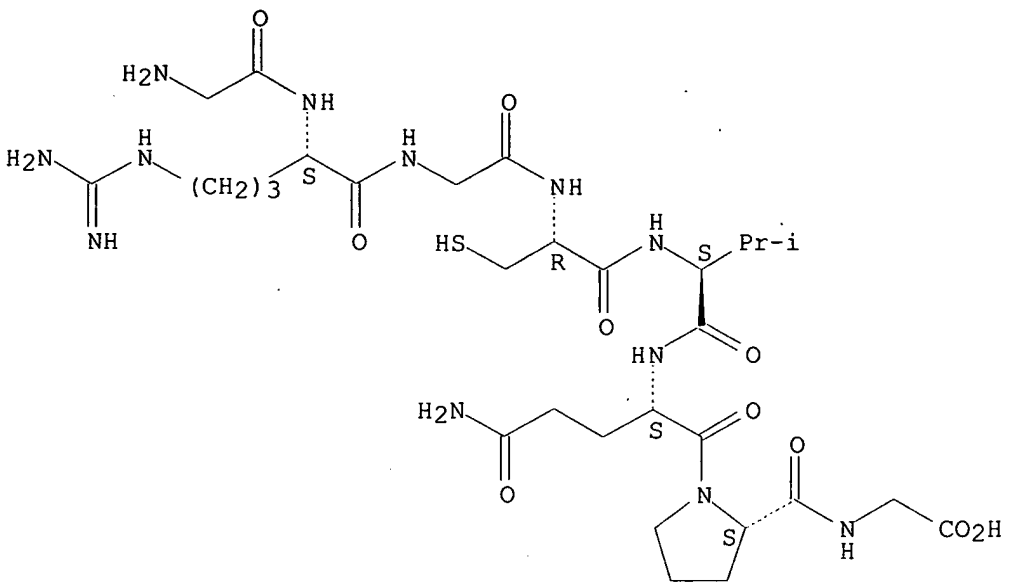
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 16 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-28-9 REGISTRY
CN Glycine,
glycyl-L-arginylglycyl-L-cysteinyl-L-valyl-L-glutaminyl-L-prolyl-
(9CI) (CA INDEX NAME)
OTHER NAMES:
CN 9: PN: WO0007609 SEQID: 9 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Arg-Gly-Cys-Val-Gln-Pro-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C30 H52 N12 O10 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

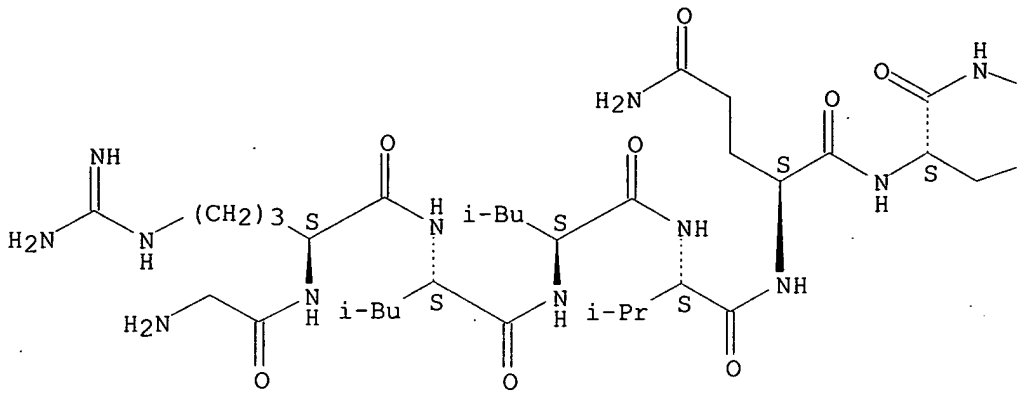
L2 ANSWER 17 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-27-8 REGISTRY
CN Glycine,
glycyl-L-arginyl-L-leucyl-L-leucyl-L-valyl-L-glutaminyl-L-.alpha.-
aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 8: PN: WO0007609 SEQID: 8 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Arg-Leu-Leu-Val-Gln-Asp-Gly
=== === === === === === === ===
HITS AT: 1-8

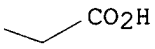
MF C36 H64 N12 O12
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

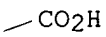
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B





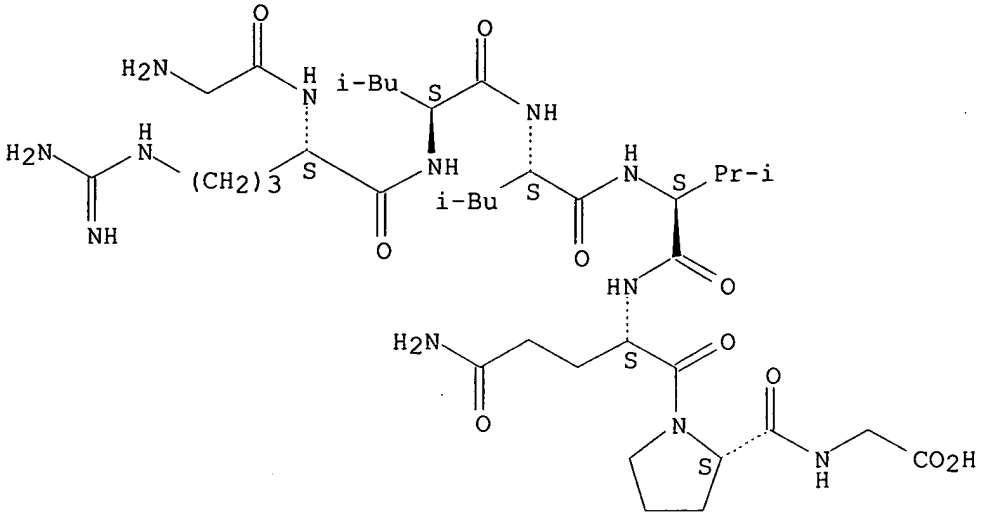
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 18 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-26-7 REGISTRY
CN Glycine,
glycyl-L-arginyl-L-leucyl-L-leucyl-L-valyl-L-glutaminyl-L-prolyl-
(9CI) (CA INDEX NAME)
OTHER NAMES:
CN 7: PN: WO0007609 SEQID: 7 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Arg-Leu-Leu-Val-Gln-Pro-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C37 H66 N12 O10
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 19 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-25-6 REGISTRY
CN Glycine, glycyl-L-arginyl-L-leucyl-L-cysteinyl-L-valyl-L-glutaminyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 6: PN: WO0007609 SEQID: 6 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 8

SEQ3 1 Gly-Arg-Leu-Cys-Val-Gln-Asp-Gly
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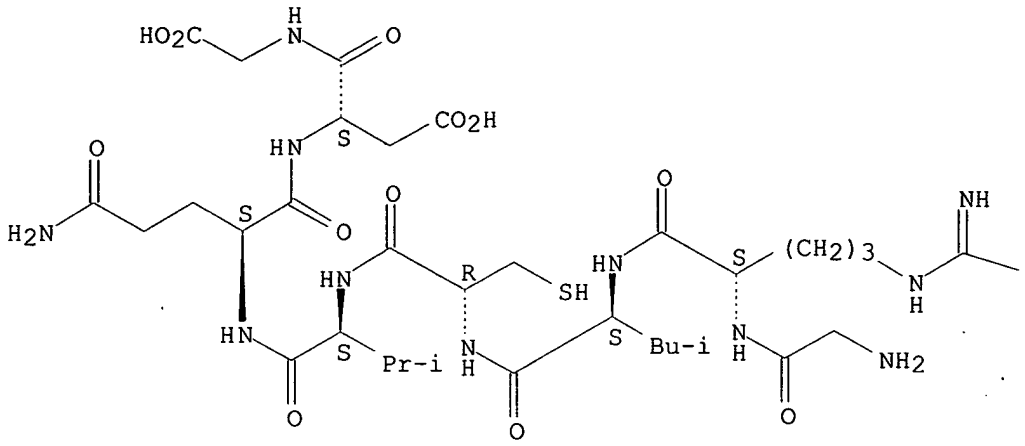
HITS AT: 1-8

MF C33 H58 N12 O12 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 20 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-24-5 REGISTRY
CN Glycine, glycyl-L-arginyl-L-leucyl-L-cysteinyl-L-valyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 5: PN: WO0007609 SEQID: 5 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Arg-Leu-Cys-Val-Gln-Pro-Gly
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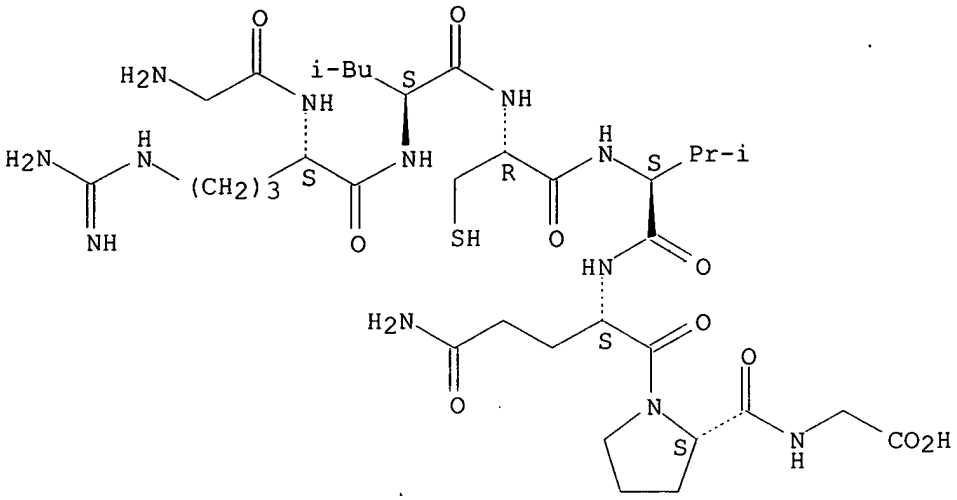
HITS AT: 1-8

MF C34 H60 N12 O10 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 21 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-23-4 REGISTRY
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glycyl-L-arginyl-L-valyl-L-leucyl-L-valyl-L-glutaminyl-L-.alpha.-
aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4: PN: WO0007609 SEQID: 4 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Arg-Val-Leu-Val-Gln-Asp-Gly
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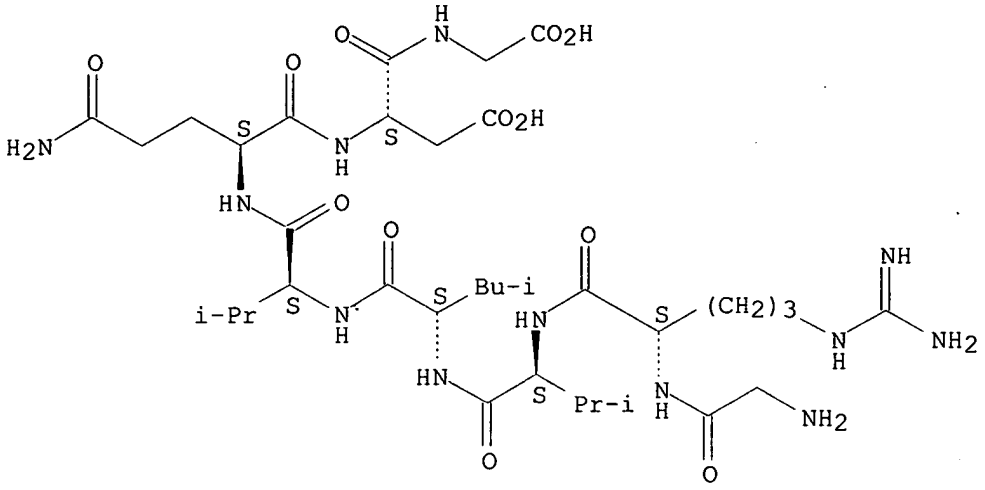
HITS AT: 1-8

MF C35 H62 N12 O12
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



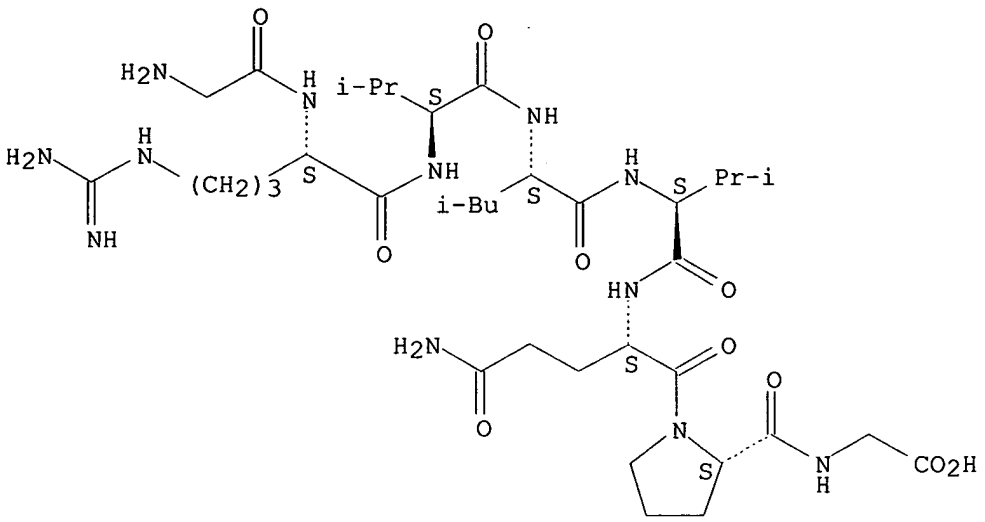
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 22 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-22-3 REGISTRY
CN Glycine, glycyl-L-arginyl-L-valyl-L-leucyl-L-valyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3: PN: WO0007609 SEQID: 3 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 8

SEQ3 1 Gly-Arg-Val-Leu-Val-Gln-Pro-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C36 H64 N12 O10
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 23 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-21-2 REGISTRY
CN Glycine, glycyl-L-arginyl-L-valyl-L-cysteinyl-L-valyl-L-glutaminyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2: PN: WO0007609 SEQID: 2 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Arg-Val-Cys-Val-Gln-Asp-Gly
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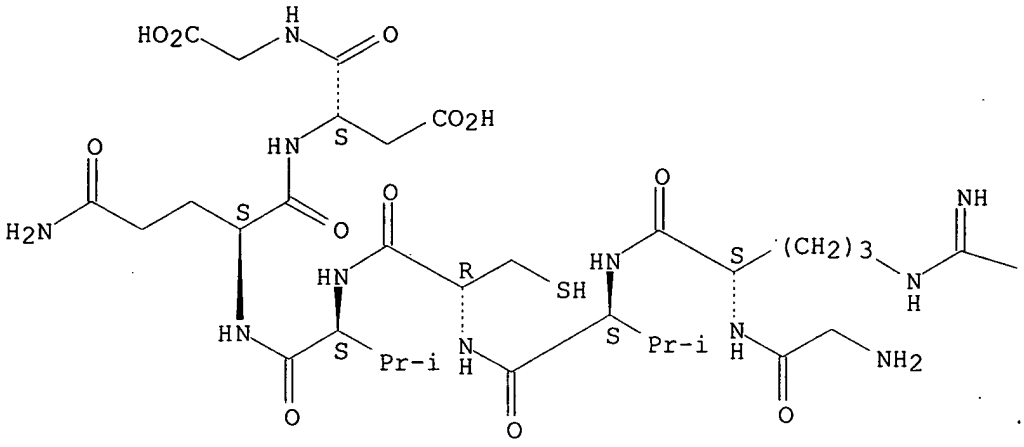
HITS AT: 1-8

MF C32 H56 N12 O12 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

NH_2

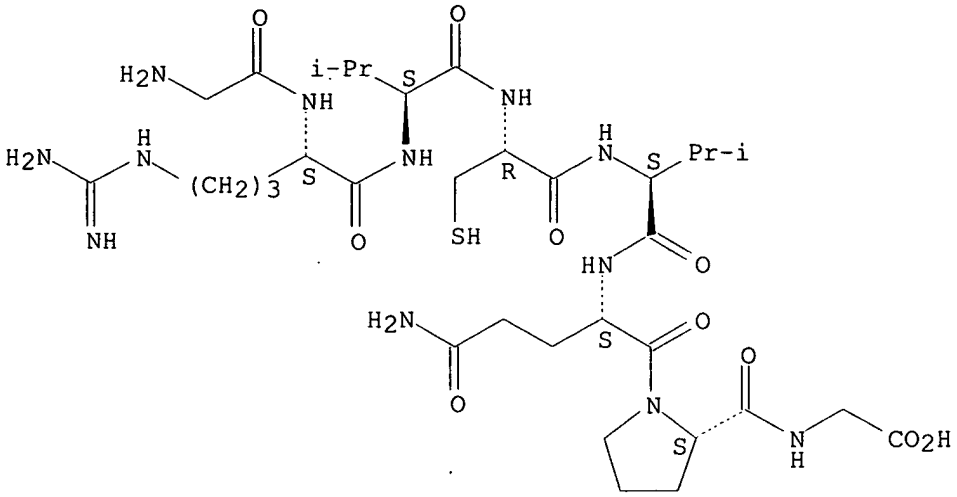
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 24 OF 24 REGISTRY COPYRIGHT 2001 ACS
RN 258818-20-1 REGISTRY
CN Glycine, glycyl-L-arginyl-L-valyl-L-cysteinyl-L-valyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1: PN: WO0007609 SEQID: 1 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **8**

SEQ3 1 Gly-Arg-Val-Cys-Val-Gln-Pro-Gly
=== === === === === === === ===
HITS AT: 1-8

MF C33 H58 N12 O10 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 08:48:33 ON 09 JUL 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1947 - 9 Jul 2001 VOL 135 ISS 3
FILE LAST UPDATED: 8 Jul 2001 (20010708/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

=> d his l3-

FILE 'HCAPLUS' ENTERED AT 08:46:20 ON 09 JUL 2001
L3 2 S L2
L4 8 S ZONULIN#
L5 8 S ZONULIN#/AB
L6 8 S L4 OR L5
L7 37 S ZONULA OCCLUDENS (L) TOXIN#
L8 7 S L7 (L) RECEPTOR#
L9 3 S L8 NOT L6

=> d .ca l3 1-2;d .ca l6 1-8;d .ca l9 1-3

L3 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:190949 HCAPLUS
DOCUMENT NUMBER: 132:246351
TITLE: Method of using zonula occludens toxin (Zot) or zonulin to inhibit lymphocyte proliferation in an antigen-specific manner
INVENTOR(S): Fasano, Alessio; Sztein, Marcelo B.; Lu, Ruiliang; Tanner, Michael K.
PATENT ASSIGNEE(S): University of Maryland, Baltimore, USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015252	A1	20000323	WO 1999-US18842	19990909
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960190	A1	20000403	AU 1999-60190	19990909
NO 2001001253	A	20010315	NO 2001-1253	20010313

PRIORITY APPLN. INFO.: US 1998-100266 P 19980914
WO 1999-US18842 W 19990909

AB Methods for using Zot or zonulin as an antigen-specific inhibitor of antigen-presenting cell (APC) activity and lymphocyte proliferation, being primarily useful in the field of immunoregulation and immunotherapy, are described. Specifically, Zot and zonulin inhibit antigen-presenting cell-mediated antigen-specific lymphocyte proliferation in a

dose-dependent manner. This effect is assocd. with the presence of a macrophage surface receptor to which Zot binds in a specific and saturable way. This down-regulation of the immune response is, at least in part, assocd. with a decreased uptake of antigen.

IC ICM A61K039-00
CC 1-7 (Pharmacology)
Section cross-reference(s): 15, 63
IT **258818-34-7** 258818-44-9
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(zonula occludens toxin or zonulin for inhibition of lymphocyte proliferation in antigen-specific manner)
REFERENCE COUNT: 1
REFERENCE(S): (1) Fasano; US 5945510 A 1999 HCAPLUS

L3 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:116910 HCAPLUS
DOCUMENT NUMBER: 132:175864
TITLE: Zonula occludens receptor-binding peptide antagonists of zonulin and methods for their use
INVENTOR(S): Fasano, Alessio
PATENT ASSIGNEE(S): University of Maryland, Baltimore, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000007609	A1	20000217	WO 1999-US16683	19990728
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9954590	A1	20000228	AU 1999-54590	19990728
EP 1102596	A1	20010530	EP 1999-940809	19990728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001000567	A	20010402	NO 2001-567	20010202

PRIORITY APPLN. INFO.: US 1998-127815 A 19980803
WO 1999-US16683 W 19990728

AB Peptide antagonists of zonulin are disclosed, as well as methods for the their use. The peptide antagonists bind to the zonula occludens receptor, yet do not physiol. modulate the opening of mammalian tight junctions. The peptide antagonists may be used e.g. to treat gastrointestinal inflammation or conditions assocd. with breakdown of the blood-brain barrier. Purifn. of zonulin and zonula occludens toxin are described.

IC ICM A61K038-00

ICS A61K038-16; A61K038-17; C07K005-00; C07K007-00; C07K014-00; C12N013-15
CC 1-12 (Pharmacology)
Section cross-reference(s): 13
IT **258818-20-1 258818-21-2 258818-22-3**
258818-23-4 258818-24-5 258818-25-6
258818-26-7 258818-27-8 258818-28-9
258818-29-0 258818-30-3 258818-31-4
258818-32-5 258818-33-6 258818-34-7
258818-35-8 258818-36-9 258818-37-0
258818-38-1 258818-39-2 258818-40-5
258818-41-6 258818-42-7 258818-43-8
258818-45-0
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zonula occludens receptor-binding peptide antagonists of zonulin, and therapeutic use)
REFERENCE COUNT: 4
REFERENCE(S):
(1) Baudry; Infection and Immunity 1992, V60(2), P428 HCAPLUS
(2) Cancer Research Fund Of Contra Costa; WO 9411509 A2 1994 HCAPLUS
(3) Fasano; US 5945510 A 1999 HCAPLUS
(4) Takara Shuzo Co Ltd; EP 0675199 A2 1995 HCAPLUS

L6 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:429813 HCAPLUS
TITLE: Zonula occludens toxin structure-function analysis. Identification of the fragment biologically active on tight junctions and of the **zonulin** receptor binding domain
AUTHOR(S): Di Pierro, Mariarosaria; Lu, Ruliang; Uzzau, Sergio; Wang, Wenle; Margaretten, Klara; Pazzani, Carlo; Maimone, Francesco; Fasano, Alessio
CORPORATE SOURCE: Division of Pediatric Gastroenterology and Nutrition and Gastrointestinal Pathophysiology Section, Center for Vaccine Development, University of Maryland School of Medicine, Baltimore, MD, 21201, USA
SOURCE: J. Biol. Chem. (2001), 276(22), 19160-19165
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Zonula occludens toxin (Zot) is an enterotoxin elaborated by Vibrio cholerae that increases intestinal permeability by interacting with a mammalian cell receptor with subsequent activation of intracellular signaling leading to the disassembly of the intercellular tight junctions.
Zot localizes in the bacterial outer membrane of V. cholerae with subsequent cleavage and secretion of a carboxyl-terminal fragment in the host intestinal milieu. To identify the Zot domain(s) directly involved in the protein permeating effect, several zot gene deletion mutants were

constructed and tested for their biol. activity in the Ussing chamber assay and their ability to bind to the target receptor on intestinal epithelial cell cultures. The Zot biol. active domain was localized toward the carboxyl terminus of the protein and coincided with the predicted cleavage product generated by V. cholerae. This domain shared a putative receptor-binding motif with **zonulin**, the Zot mammalian analog involved in tight junction modulation. Amino acid comparison between the Zot active fragment and **zonulin**, combined with site-directed mutagenesis expts., confirmed the presence of an octapeptide receptor-binding domain toward the amino terminus of the processed Zot.

CC 4 (Toxicology)
REFERENCE COUNT: 32
REFERENCE(S):
(1) Anderson, J; J Cell Biol 1993, V5, P772 HCAPLUS
(2) Baudry, B; Infect Immun 1992, V60, P428 HCAPLUS
(5) Fanning, A; J Biol Chem 1998, V273, P29745 HCAPLUS
(6) Fasano, A; Gastroenterology 1997, V112, P839 HCAPLUS
(7) Fasano, A; J Clin Invest 1995, V96, P710 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:70444 HCAPLUS
DOCUMENT NUMBER: 134:248016
TITLE: Regulation of intercellular tight junctions by zonula occludens toxin and its eukaryotic analogue **zonulin**
AUTHOR(S): Fasano, Alessio
CORPORATE SOURCE: Division of Pediatric Gastroenterology and Nutrition, University of Maryland School of Medicine, Baltimore, MD, 21201, USA
SOURCE: Ann. N. Y. Acad. Sci. (2000), 915(Epithelial Transport and Barrier Function), 214-222
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review and discussion with 60 refs. The intestinal epithelium represents the largest interface between the external environment and the internal host milieu and constitutes the major barrier through which mols. can either be absorbed or secreted. There is now substantial evidence that tight junctions (tj) play a major role in regulating epithelial permeability by influencing paracellular flow of fluid and solutes. Tj are one of the hallmarks of absorptive and secretory epithelia. Evidence now exists that tj are dynamic rather than static structures and readily adapt to a variety of developmental, physiol., and pathol. circumstances. These adaptive mechanisms are still incompletely understood. Activation of PKC either by Zonula occludens toxin (Zot) or by phorbol esters increases paracellular permeability. Alteration of epithelial tj is a recently described property for infectious agents. Clostridium difficile toxin A and B and influenza and vesicular stomatitis viruses have been shown to loosen tj in tissue culture monolayers. Unlike what occurs after

the Zot stimulus, these changes appear to be irreversible and are assocd. with destruction of the tj complex. On the basis of this observation, we postulated that Zot may mimic the effect of a functionally and immunol. related endogenous modulator of epithelial tj. The author's group was able to identify an intestinal Zot analog, which we named **zonulin** . It is conceivable that the **zonulins** participate in the physiol. regulation of intercellular tj not only in the small intestine, but also throughout a wide range of extra-intestinal epithelia as well as the ubiquitous vascular endothelium, including the blood-brain barrier. Disregulation of this hypothetical **zonulin** model may contribute to disease states that involve disordered intercellular communication, including developmental and intestinal disorders, tissue inflammation, malignant transformation, and metastasis.

CC 4-0 (Toxicology)
Section cross-reference(s): 14

ST intercellular tight junction zonula occludens toxin eukaryote **zonulin** review

IT Eukaryote (Eukaryotae)
(intercellular tight junctions regulation by zonula occludens toxin and its eukaryotic analog **zonulin**)

IT Toxins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(intercellular tight junctions regulation by zonula occludens toxin and its eukaryotic analog **zonulin**)

IT Cell junction
(tight junction; intercellular tight junctions regulation by zonula occludens toxin and its eukaryotic analog **zonulin**)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**zonulins**; intercellular tight junctions regulation by zonula occludens toxin and its eukaryotic analog **zonulin**)

REFERENCE COUNT: 62
REFERENCE(S):
(1) Anderson, J; Curr Biol 1996, V6, P382 HCAPLUS
(2) Bakker, R; Am J Physiol 1984, V246, PG213 HCAPLUS
(3) Balda, M; J Cell Sci 1998, V111, P541 HCAPLUS
(4) Citi, S; Nature (London) 1988, V333, P272 HCAPLUS
(5) Denker, B; Am J Physiol 1998, V274, PF1-9 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:64654 HCAPLUS
DOCUMENT NUMBER: 134:234809
TITLE: Human **zonulin**, a potential modulator of intestinal tight junctions
AUTHOR(S): Wang, Wenle; Uzzau, Sergio; Goldblum, Simeon E.; Fasano, Alessio
CORPORATE SOURCE: Division of Pediatric Gastroenterology and Nutrition and Gastrointestinal Pathophysiology Section, Center for Vaccine Development, Department of Veterans Affairs Medical Center, School of Medicine, University of Maryland, Baltimore, MD, 21201, USA
SOURCE: J. Cell Sci. (2000), 113(24), 4435-4440
CODEN: JNCSAI; ISSN: 0021-9533

PUBLISHER: Company of Biologists Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Intercellular tight junctions are dynamic structures involved in vectorial transport of water and electrolytes across the intestinal epithelium. Zonula occludens toxin derived from Vibrio cholerae interacts with a specific intestinal epithelial surface receptor, with subsequent activation of a complex intracellular cascade of events that regulate tight junction permeability. We postulated that this toxin may mimic the effect of a functionally and immunol. related endogenous modulator of intestinal tight junctions. Affinity-purified anti-zonula occludens toxin antibodies and the Ussing chamber assay were used to screen for one or more mammalian zonula occludens toxin analogs in both fetal and adult human intestine. A novel protein, **zonulin**, was identified that induces tight junction disassembly in non-human primate intestinal epithelia mounted in Ussing chambers. Comparison of amino acids in the active zonula occludens toxin fragment and **zonulin** permitted the identification of the putative receptor binding domain within the N-terminal region of the two proteins. **Zonulin** likely plays a pivotal role in tight junction regulation during developmental, physiol., and pathol. processes, including tissue morphogenesis, movement of fluid, macromols. and leukocytes between the intestinal lumen and the interstitium, and inflammatory/autoimmune disorders.
CC 13-2 (Mammalian Biochemistry)
Section cross-reference(s): 10
ST **zonulin** zonula occludens toxin intestine tight junction permeability fetus
IT Protein motifs
(N-terminus, of **zonulin** and Zot; human **zonulin**, potential modulator of intestinal tight junctions)
IT New natural products
(**Zonulin** (protein))
IT Toxins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(Zot (zonula occludens toxin); human **zonulin**, potential modulator of intestinal tight junctions in comparison with)
IT Protein receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(binding; human **zonulin**, potential modulator of intestinal tight junctions)
IT Intestine
(epithelium; human **zonulin**, potential modulator of intestinal tight junctions)
IT Embryo, animal
(fetus; human **zonulin**, potential modulator of intestinal tight junctions)
IT Brain
Heart
(human **zonulin**, potential modulator of intestinal tight junctions)
IT Vibrio cholerae
(human **zonulin**, potential modulator of intestinal tight junctions in comparison with)
IT Biological transport

(permeation; human **zonulin**, potential modulator of intestinal tight junctions)
IT Protein motifs
(receptor binding; human **zonulin**, potential modulator of intestinal tight junctions)
IT Cell junction
(tight junction; human **zonulin**, potential modulator of intestinal tight junctions)
IT Protein receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(zonula occludens toxin receptor; human **zonulin**, potential modulator of intestinal tight junctions)
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(**zonulin**; human **zonulin**, potential modulator of intestinal tight junctions)
IT 330187-26-3
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(receptor-binding motif; human **zonulin**, potential modulator of intestinal tight junctions)
REFERENCE COUNT: 24
REFERENCE(S): (2) Baudry, B; Infect Immun 1992, V60, P428 HCAPLUS
(5) Fasano, A; Gastroenterology 1997, V112, P839 HCAPLUS
(6) Fasano, A; J Clin Invest 1995, V96, P710 HCAPLUS
(7) Fasano, A; Lancet 2000, V355, P1518 HCAPLUS
(8) Fasano, A; Proc Natl Acad Sci USA 1991, V88, P5242 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:322659 HCAPLUS
DOCUMENT NUMBER: 133:279924
TITLE: **Zonulin**, a newly discovered modulator of intestinal permeability, and its expression in celiac disease
AUTHOR(S): Fasano, A.; Not, T.; Wang, W.; Uzzau, S.; Berti, I.; Tommasini, A.; Goldblum, S. E.
CORPORATE SOURCE: Center for Vaccine Development, and Gastrointestinal Pathophysiology Section, Division of Paediatric Gastroenterology and Nutrition, School of Medicine, University of Maryland, Baltimore, MD, 21201, USA
SOURCE: Lancet (2000), 355(9214), 1518-1519
CODEN: LANCAO; ISSN: 0140-6736
PUBLISHER: Lancet Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We identified **zonulin**, a novel human protein analog to the Vibrio cholerae derived Zonula occludens toxin, which induces tight junction disassembly and a subsequent increase in intestinal permeability in non-human primate intestinal epithelium. **Zonulin** expression was raised in intestinal tissues during the acute phase of coeliac

disease, a clin. condition in which tight junctions are opened and permeability is increased.
CC 14-7 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 15
ST **zonulin** IgA IgG intestine permeability celiac disease
IT Immunoglobulins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(A; **zonulin**, a newly discovered modulator of intestinal permeability, and its expression in celiac disease in relation to)
IT Immunoglobulins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(G; **zonulin**, a newly discovered modulator of intestinal permeability, and its expression in celiac disease in relation to)
IT Intestine
(epithelium; **zonulin**, a newly discovered modulator of intestinal permeability, and its expression in celiac disease)
IT Intestine
(permeability of; **zonulin**, a newly discovered modulator of intestinal permeability, and its expression in celiac disease)
IT Cell junction
(tight junction; **zonulin**, a newly discovered modulator of intestinal permeability, and its expression in celiac disease)
IT Toxins
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BIOL (Biological study); PROC (Process)
(zonula occludens; **zonulin**, a newly discovered modulator of intestinal permeability, and its expression in celiac disease)
IT Celiac disease
(**zonulin**, a newly discovered modulator of intestinal permeability, and its expression in celiac disease)
IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BIOL (Biological study); PROC (Process)
(**zonulin**; **zonulin**, a newly discovered modulator of intestinal permeability, and its expression in celiac disease)
REFERENCE COUNT: 5
REFERENCE(S):
(1) Fasano, A; Gastroenterology 1997, V112, P839 HCAPLUS
(2) Larkin, M; Lancet 1997, V349, P1676 MEDLINE
(3) Meddings, J; Am J Physiol 1999, V276, PG951 HCAPLUS
(4) Schulzke, J; Pediatr Res 1998, V43, P435 MEDLINE
(5) Ventura, A; Gastroenterology 1999, V117, P303

L6 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:190949 HCAPLUS
DOCUMENT NUMBER: 132:246351
TITLE: Method of using zonula occludens toxin (Zot) or **zonulin** to inhibit lymphocyte proliferation in an antigen-specific manner
INVENTOR(S): Fasano, Alessio; Sztein, Marcelo B.; Lu, Ruiliang; Tanner, Michael K.
PATENT ASSIGNEE(S): University of Maryland, Baltimore, USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015252	A1	20000323	WO 1999-US18842	19990909
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960190	A1	20000403	AU 1999-60190	19990909
NO 2001001253	A	20010315	NO 2001-1253	20010313

PRIORITY APPLN. INFO.: US 1998-100266 P 19980914
WO 1999-US18842 W 19990909

AB Methods for using Zot or **zonulin** as an antigen-specific inhibitor of antigen-presenting cell (APC) activity and lymphocyte proliferation, being primarily useful in the field of immunoregulation and immunotherapy, are described. Specifically, Zot and **zonulin** inhibit antigen-presenting cell-mediated antigen-specific lymphocyte proliferation in a dose-dependent manner. This effect is assocd. with the presence of a macrophage surface receptor to which Zot binds in a specific and saturable way. This down-regulation of the immune response is, at least in part, assocd. with a decreased uptake of antigen.

IC ICM A61K039-00

CC 1-7 (Pharmacology)
Section cross-reference(s): 15, 63

ST zonula occludens toxin immunosuppressant lymphocyte proliferation; Zot **zonulin** immunosuppressant lymphocyte proliferation; antigen presenting cell Zot **zonulin** immunosuppressant; immune disease treatment Zot **zonulin**

IT Antitumor agents
(Kaposi's sarcoma; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(MBP (maltose-binding protein), fusion products, with zonula occludens toxin; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Tumor necrosis factors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(TNF-.alpha.; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Testis, disease
(autoimmune orchitis; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Thyroid gland, disease

(autoimmune thyroiditis; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Infection
(bacterial, inflammation assocd. with; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Bronchi
(bronchial-assocd. lymphoid tissue; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Blood coagulation
(disorder, autoimmune; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Immunity
(disorder; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Equus asinus
(donkey; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Intestine
(epithelium; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Drugs
(gastrointestinal; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Reproductive tract
(genital-assocd. lymphoid tissue; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Anemia (disease)
(hemolytic; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Purpura (disease)
(idiopathic thrombocytopenic; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Parasite
(infection, inflammation assocd. with; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Mycosis
(inflammation assocd. with; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Allergens
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inflammation-related; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Intestine, disease
(inflammatory; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Cell proliferation
(inhibitors; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Drug delivery systems
(injections, i.m.; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Drug delivery systems

(injections, i.v.; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Drug delivery systems
(injections, s.c.; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Drug delivery systems
(intradermal; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Cell proliferation
(lymphocyte; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Drug delivery systems
(mucosal; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Nose
(nasal-assocd. lymphoid tissue; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Nerve, disease
(neuritis, polyneuritis; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Drug delivery systems
(parenterals; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Skin, disease
(pemphigus; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Anemia (disease)
(pernicious anemia; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Muscle, disease
(polymyositis; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Lymphocyte
(proliferation; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Heart, disease
(rheumatic carditis; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Connective tissue
(scleroderma; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Cell proliferation
(smooth muscle cell proliferative disease; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Muscle
(smooth, smooth muscle cell proliferative disease; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Lupus erythematosus
(systemic; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Toxoids
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(tetanus; zonula occludens toxin or **zonulin** for inhibition of

lymphocyte proliferation in antigen-specific manner)
IT Multiple sclerosis
(therapeutic agents; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Antigens
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transplantation antigens; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Biological transport
(uptake; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Blood vessel, disease
(vasculitis; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Infection
(viral, inflammation assocd. with; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT Addison's disease
Allergy inhibitors
Animal tissue culture
Anti-inflammatory agents
Antiasthmatics
Antidiabetic agents
Antigen-presenting cell
Antirheumatic agents
Autoimmune disease
B cell (lymphocyte)
Bison bison
Cardiovascular agents
Cat (Felis catus)
Cattle
Celiac disease
Deer
Dermatomyositis
Dog (Canis familiaris)
Drug delivery systems
Eczema
Goat
Graves' disease
Horse (Equus caballus)
Immunosuppressants
Lymphatic system
Macrophage
Monocyte
Mononuclear cell (leukocyte)
Myasthenia gravis
Primate
Psoriasis
Sheep
Sjogren's syndrome
Swine
T cell (lymphocyte)
Tonsil
Transplant rejection
(zonula occludens toxin or **zonulin** for inhibition of

lymphocyte proliferation in antigen-specific manner)

IT Phytohemagglutinins
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Antigens
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT CD14 (antigen)
Interleukin 10
Interleukin 1.beta.
Interleukin 2
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**zonulin**; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT Interferons
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.gamma.; zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT 261943-83-3
RL: PRP (Properties)
(Unclaimed; method of using zonula occludens toxin (Zot) or **zonulin** to inhibit lymphocyte proliferation in an antigen-specific manner)

IT 198041-73-5, 1: PN: WO0007609 SEQID: 25 unclaimed DNA 198041-74-6, 2: PN: WO0007609 SEQID: 26 unclaimed DNA 259126-67-5, 3: PN: WO0007609 SEQID: 39 unclaimed DNA 259126-68-6, 4: PN: WO0007609 SEQID: 40 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; method of using zonula occludens toxin (Zot) or **zonulin** to inhibit lymphocyte proliferation in an antigen-specific manner)

IT 262282-03-1
RL: PRP (Properties)
(unclaimed protein sequence; method of using zonula occludens toxin (Zot) or **zonulin** to inhibit lymphocyte proliferation in an antigen-specific manner)

IT 258818-34-7 258818-44-9
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)

IT 50812-37-8DP, Glutathione-S-transferase, zonula occludens toxin fusion products
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
IT 9004-54-0D, Dextran, FITC conjugates 27072-45-3D, FITC, dextran conjugates
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(zonula occludens toxin or **zonulin** for inhibition of lymphocyte proliferation in antigen-specific manner)
REFERENCE COUNT: 1
REFERENCE(S): (1) Fasano; US 5945510 A 1999 HCAPLUS

L6 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:116910 HCAPLUS
DOCUMENT NUMBER: 132:175864
TITLE: Zonula occludens receptor-binding peptide antagonists of **zonulin** and methods for their use
INVENTOR(S): Fasano, Alessio
PATENT ASSIGNEE(S): University of Maryland, Baltimore, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000007609	A1	20000217	WO 1999-US16683	19990728
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9954590	A1	20000228	AU 1999-54590	19990728
EP 1102596	A1	20010530	EP 1999-940809	19990728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001000567	A	20010402	NO 2001-567	20010202

PRIORITY APPLN. INFO.: US 1998-127815 A 19980803
WO 1999-US16683 W 19990728

AB Peptide antagonists of **zonulin** are disclosed, as well as methods for the their use. The peptide antagonists bind to the zonula occludens receptor, yet do not physiol. modulate the opening of mammalian tight junctions. The peptide antagonists may be used e.g. to treat gastrointestinal inflammation or conditions assocd. with breakdown of the blood-brain barrier. Purifn. of **zonulin** and zonula occludens toxin are described.

IC ICM A61K038-00
ICS A61K038-16; A61K038-17; C07K005-00; C07K007-00; C07K014-00; C12N013-15

CC 1-12 (Pharmacology)
Section cross-reference(s): 13
ST **zonulin** peptide antagonist therapeutic; zonula occludens receptor peptide antagonist therapeutic; gastrointestinal inflammation **zonulin** peptide antagonist; blood brain barrier **zonulin** peptide antagonist
IT Blood-brain barrier
(condition assocd. with breakdown of; zonula occludens receptor-binding
peptide antagonists of **zonulin**, and therapeutic use)
IT Anti-inflammatory agents
(gastrointestinal inflammation; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)
IT Drugs
(gastrointestinal, for gastrointestinal inflammation; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)
IT Cell junction
(tight junction; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)
IT Antibodies
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(to zonula occludens toxin (ZOT); zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)
IT Biological transport
Protein sequences
(zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)
IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)
IT Toxins
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(zonula occludens toxin (ZOT); zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)
IT Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(zonula occludens toxin receptor; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)
IT Brain
Heart
Intestine
(**zonulin** from; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)
IT Proteins, specific or class
RL: BPR (Biological process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**zonulin**; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)
IT 216435-13-1
RL: PRP (Properties)
(adult human brain **zonulin** amino-terminal fragment; zonula occludens receptor-binding peptide antagonists of **zonulin**,

and therapeutic use)

IT 216435-12-0
RL: PRP (Properties)
(adult human heart **zonulin** amino-terminal fragment; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)

IT 216435-15-3
RL: PRP (Properties)
(adult human heart **zonulin** fragment; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)

IT 258871-79-3
RL: PRP (Properties)
(adult human intestine **zonulin** amino-terminal fragment; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)

IT 258871-75-9
RL: PRP (Properties)
(fetal human brain **zonulin** amino-terminal fragment; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)

IT 216491-91-7
RL: PRP (Properties)
(fetal human intestine **zonulin** amino-terminal fragment; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)

IT 9004-10-8, Insulin, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(intestinal absorption; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)

IT 216435-11-9
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(rabbit intestine **zonulin** amino-terminal fragment; zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)

IT 198041-73-5, 1: PN: WO0007609 SEQID: 25 unclaimed DNA 198041-74-6, 2: PN: WO0007609 SEQID: 26 unclaimed DNA 259126-67-5, 3: PN: WO0007609 SEQID: 39 unclaimed DNA 259126-68-6, 4: PN: WO0007609 SEQID: 40 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; zonula occludens receptor-binding peptide antagonists of **zonulin** and methods for their use)

IT 259085-43-3 259085-44-4
RL: PRP (Properties)
(unclaimed sequence; zonula occludens receptor-binding peptide antagonists of **zonulin** and methods for their use)

IT 258818-44-9
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)

IT 258818-20-1 258818-21-2 258818-22-3 258818-23-4 258818-24-5
258818-25-6 258818-26-7 258818-27-8 258818-28-9 258818-29-0
258818-30-3 258818-31-4 258818-32-5 258818-33-6 258818-34-7
258818-35-8 258818-36-9 258818-37-0 258818-38-1 258818-39-2
258818-40-5 258818-41-6 258818-42-7 258818-43-8 258818-45-0

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)

IT 258872-04-7
RL: PRP (Properties)
(zonula occludens receptor-binding peptide antagonists of **zonulin**, and therapeutic use)

REFERENCE COUNT: 4
REFERENCE(S):
(1) Baudry; Infection and Immunity 1992, V60(2), P428 HCAPLUS
(2) Cancer Research Fund Of Contra Costa; WO 9411509 A2 1994 HCAPLUS
(3) Fasano; US 5945510 A 1999 HCAPLUS
(4) Takara Shuzo Co Ltd; EP 0675199 A2 1995 HCAPLUS

L6 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:5303 HCAPLUS
DOCUMENT NUMBER: 132:133833
TITLE: Affinity purification and partial characterization of the **zonulin**/zonula occludens toxin (Zot) receptor from human brain
AUTHOR(S): Lu, R.; Wang, W.; Uzzau, S.; Vigorito, R.; Zielke, H. R.; Fasano, A.
CORPORATE SOURCE: Division of Pediatric Gastroenterology and Nutrition and Center for Vaccine Development, University of Maryland School of Medicine, Baltimore, MD, 21201, USA
SOURCE: J. Neurochem. (2000), 74(1), 320-326
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The intercellular tight junctions (TJs) of endothelial cells represent the limiting structure for the permeability of the blood-brain barrier (BBB). Although the BBB has been recognized as being the interface between the bloodstream and the brain, little is known about its regulation. **Zonulin** and its prokaryotic analog, zonula occludens toxin (Zot) elaborated by Vibrio cholerae, both modulate intercellular TJs by binding to a sp. surface receptor with subsequent activation of an intracellular signaling pathway involving phospholipase C and protein kinase C activation and actin polymn. Affinity column purifn. revealed that human brain plasma membrane prepns. contain two Zot binding proteins of .apprx.55 and .apprx.45 kDa. Structural and kinetic studies, including satn. and competitive assays, identified the 55-kDa protein as tubulin, whereas the 45-kDa protein represents the **zonulin**/Zot receptor. Biochem. characterization provided evidence that this receptor is a glycoprotein contg. multiple sialic acid residues. Comparison of the N-terminal sequence of the **zonulin**/Zot receptor with other protein sequences by BLAST anal. revealed a striking similarity with MRP-8, a 14-kDa member of the S-100 family of calcium binding proteins. The discovery and characterization of this receptor from human brain may significantly contribute to our knowledge on the pathophysiol. regulation of the BBB.

CC 6-3 (General Biochemistry)
Section cross-reference(s): 4, 13

ST **zonulin** zonula occludens toxin receptor protein brain human
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study) (MRP-8 (migration-inhibiting factor-related, 8000-mol.-wt.); affinity purifn. and partial characterization of **zonulin**/zonula occludens toxin (Zot) receptor from human brain)
IT Proteins, specific or class
RL: BOC (Biological occurrence); BPR (Biological process); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process) (Zot binding protein; affinity purifn. and partial characterization of **zonulin**/zonula occludens toxin (Zot) receptor from human brain)
IT Blood-brain barrier
Brain
Heart
Intestine
Protein sequences
(affinity purifn. and partial characterization of **zonulin** /zonula occludens toxin (Zot) receptor from human brain)
IT Cell junction
(tight junction; affinity purifn. and partial characterization of **zonulin**/zonula occludens toxin (Zot) receptor from human brain)
IT Receptors
RL: BOC (Biological occurrence); BPR (Biological process); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process) (**zonulin**/zonula occludens toxin; affinity purifn. and partial characterization of **zonulin**/zonula occludens toxin (Zot) receptor from human brain)
IT Toxins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (**zonulin**/zonula occludens toxin; affinity purifn. and partial characterization of **zonulin**/zonula occludens toxin (Zot) receptor from human brain)
REFERENCE COUNT: 30
REFERENCE(S): (2) Baudry, B; Infect Immun 1992, V60, P428 HCAPLUS
(4) Denker, B; Am J Physiol 1998, V274, PF1 HCAPLUS
(6) Dorin, J; Nature 1987, V326, P614 HCAPLUS
(7) Fasano, A; Am J Physiol 1999, V276, PC765 HCAPLUS
(8) Fasano, A; Gastroenterology 1997, V112, P839 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:776621 HCAPLUS
DOCUMENT NUMBER: 130:43300
TITLE: Substantially pure **zonulin**, a physiological modulator of mammalian tight junctions for drug delivery
INVENTOR(S): Fasano, Alessio
PATENT ASSIGNEE(S): University of Maryland, Baltimore, USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9852415	A1	19981126	WO 1998-US7636	19980428
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5945510	A	19990831	US 1997-859931	19970521
AU 9872491	A1	19981211	AU 1998-72491	19980428
EP 982988	A1	20000308	EP 1998-919778	19980428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-859931 19970521
WO 1998-US7636 19980428

AB A substantially pure mammalian protein, hereinafter "**zonulin**," that is a physiol. modulator of mammalian tight junctions is disclosed, as well as methods for the use of the same for drug delivery.

IC ICM A01N037-18
ICS A61K038-00; A61K038-28; C07K001-00; C07K014-00; C07K017-00

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 2, 15

ST **zonulin** tight junction permeation drug delivery

IT Fusion proteins (chimeric proteins)
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(ZOT-MBP; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT Antibodies
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(anti-.tau.; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT Tau factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibodies binding; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT Peptides, biological studies
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(biol. active; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT Uptake (biological)
(enhancement of; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT Proteins (specific proteins and subclasses)
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(maltose-binding, fusion proteins with zonula occludens toxin; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT Hormones (animal), biological studies
RL: BPR (Biological process); PEP (Physical, engineering or chemical

process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(peptides; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT Antibiotics
Antitumor agents
Blood-brain barrier
Cardiovascular agents
Drug delivery systems
Genetic vectors
Intravenous injections
Molecular cloning
Nasal drug delivery systems
Nervous system agents
Oral drug delivery systems
Protein sequences
Purification
Tight junction
Vaccines
(substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT Albumins, biological studies
Globulins, biological studies
IgA
IgG
IgM
Immunoglobulins
Interferon .alpha.
Interferon .beta.
Interferon .gamma.
Interleukin 1
Interleukin 2
Interleukin 4
Interleukin 8
Lymphokines
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT Antibodies
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(zonula occludens toxin-binding; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(zonula occludens, antibodies to; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT New natural products
(**zonulin** (protein))

IT Proteins (specific proteins and subclasses)
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**zonulin**; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)

IT Vibrio cholerae
(zot gene of; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)
IT Genes (microbial)
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(zot, of Vibrio cholerae; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)
IT 50-60-2, Phentolamine 51-41-2, Norepinephrine 51-43-4, Epinephrine 51-61-6, Dopamine, biological studies 57-22-7, Vincristine 58-22-0, Testosterone 58-61-7, Adenosine, biological studies 61-32-5, Methicillin 62-90-8, Nandrolin 137-58-6, Lidocaine 147-94-4, Cytarabine 306-40-1, Succinylcholine 309-29-5, Doxapram 465-65-6, Naloxone 865-21-4, Vinblastine 1404-00-8, Mitomycin 2078-54-8, Propofol 9004-10-8, Insulin, biological studies 20594-83-6, Nalbuphine 23214-92-8, Doxorubicin 34368-04-2, Dobutamine 35607-66-0, Cefoxitin 51481-65-3, Mezlocillin 52485-79-7, Buprenorphine 53648-55-8, Dezocine 56796-20-4, Cefmetazole 59467-70-8, Midazolam 61270-58-4, Cefonicid 61477-96-1, Piperacillin 61489-71-2, Menotropin 71195-58-9, Alfentanil 74103-06-3, Ketorolac 78110-38-0, Aztreonam 97048-13-0, Urofollitropin 133814-19-4, Mivacurium
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)
IT 216435-11-9 216435-12-0 216435-13-1 216435-14-2 216435-15-3 216491-91-7
RL: BOC (Biological occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(**zonulin** fragment; substantially pure **zonulin**, a physiol. modulator of mammalian tight junctions for drug delivery)
REFERENCE COUNT: 2
REFERENCE(S): (1) Baudry; Infection and Immunity 1992, V60(2), P428 HCAPLUS
(2) Fasano; US 5665389 A 1997 HCAPLUS

L9 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:23937 HCAPLUS
DOCUMENT NUMBER: 134:262480
TITLE: Purification and preliminary characterization of the **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines
AUTHOR(S): Uzzau, S.; Lu, R.; Wang, W.; Fiore, C.; Fasano, A.
CORPORATE SOURCE: Division of Pediatric Gastroenterology and Nutrition and Gastrointestinal Pathophysiology Section, Center for Vaccine Development, School of Medicine, University of Maryland, Baltimore, MD, 21201, USA
SOURCE: FEMS Microbiol. Lett. (2001), 194(1), 1-5

CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study, we report the preliminary characterization of the epithelial cell receptor for Vibrio cholerae zonula occludens toxin (Zot).

Zot receptor was purified by ligand-affinity chromatog. Anal. of affinity-purified prepns. by PAGE revealed a protein of .apprx.66 kDa. Partial N-terminal sequence obtained from purified murine and human Zot receptor revealed homol. between the two proteins and with human .alpha.-1-chimaerin. Zot protein domain(s) involved in receptor binding were also analyzed by constructing several in frame deletion derivs. of a recombinant fusion Zot protein tagged with maltose binding protein. Our results suggest that Zot binding to its cellular membrane receptor requires a sequence that spans between amino acids 118 and 299.

CC 6-3 (General Biochemistry)
Section cross-reference(s): 10

IT Proteins, specific or class
RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation)
(Murine Zot binding protein; purifn. and preliminary characterization of **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines)

IT Protein motifs
(N-terminal sequences of Zot **receptor**; purifn. and preliminary characterization of **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines)

IT Protein sequences
(N-terminal sequences of Zot **receptors**; purifn. and preliminary characterization of **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines)

IT **Toxins**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(Zot (Vibrio cholerae **zonula occludens toxin**) **receptors**; purifn. and preliminary characterization of **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines)

IT **Receptors**
RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation)
(Zot (Vibrio cholerae **zonula occludens toxin**) **receptors**; purifn. and preliminary characterization of **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines)

IT Intestine
(epithelium; purifn. and preliminary characterization of **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines)

IT Proteins, specific or class
RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation)
(human Zot binding protein; purifn. and preliminary characterization of **zonula occludens toxin receptor**

from human (CaCo2) and murine (IEC6) intestinal cell lines)
IT Cell membrane
(**receptor**; purifn. and preliminary characterization of **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines)
IT Cell junction
(tight junction, Zot (vibrio cholerae **zonula occludens toxin**) **receptors**; purifn. and preliminary characterization of **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines)
IT Vibrio cholerae
(**zonula occludens toxin receptors**; purifn. and preliminary characterization of **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines)
IT Proteins, specific or class
RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation)
(.alpha.1-chimaerins; purifn. and preliminary characterization of **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines)
REFERENCE COUNT: 17
REFERENCE(S): (2) Dong, J; Eur J Biochem 1995, V227, P636 HCAPLUS
(3) Fasano, A; Gastroenterology 1997, V112, P839 HCAPLUS
(5) Fasano, A; J Clin Invest 1995, V96, P710 HCAPLUS
(6) Fasano, A; J Pediatr Gastroenterol Nutr 1998, V26, P520 HCAPLUS
(7) Fasano, A; Lancet 2000, V355, P1518 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:384022 HCAPLUS
DOCUMENT NUMBER: 131:15465
TITLE: Human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists
INVENTOR(S): Fasano, Alessio
PATENT ASSIGNEE(S): University of Maryland, Baltimore, USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 803,364.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5912323	A	19990615	US 1998-24198	19980217
US 5864014	A	19990126	US 1997-803364	19970220
WO 9837096	A1	19980827	WO 1998-US2257	19980218

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9862702 A1 19980909 AU 1998-62702 19980218
EP 1007553 A1 20000614 EP 1998-904957 19980218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
US 5948629 A 19990907 US 1998-186409 19981105
PRIORITY APPLN. INFO.: US 1997-803364 A2 19970220
US 1998-24198 A 19980217
WO 1998-US2257 W 19980218

AB Claimed are purified receptors for the zonula occludens toxin (ZOT) of Vibrio cholerae, including protein sequences, as well as methods involving the use of the same to screen for an agonist or antagonist of the toxin.

IC ICM C07K014-705
ICS C07K014-435; C07K014-00
NCL 530350000
CC 6-3 (General Biochemistry)
Section cross-reference(s): 4, 13
ST human ZOT **toxin receptor** drug screening; **zonula occludens toxin receptor** sequence binding; tight junction **toxin receptor** sequence binding; agonist antagonist **toxin receptor** screening

IT Actins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(F-, effect of ZOT on; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ZO-1, effect of ZOT on distribution of; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT **Toxins**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(ZOT (**zonula occludens toxin**), tight junction; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT Antiserums
(anti-ZOT; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT Drug screening
Molecular association
Vibrio cholerae
(human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT Protein sequences
(of human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae)

IT Cell junction

(tight junction; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT Protein **receptors**
RL: BUU (Biological use, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**zonula occludens toxin**/tight junction **toxin**; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT **Receptors**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**zonula occludens toxin**; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT 212197-68-7 212197-69-8
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT 212197-67-6P
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); PRP (Properties); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT 9001-86-9, Phospholipase C
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(play a role in ZOT-induced actin reorganization; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT 141436-78-4, Protein kinase C
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.alpha., as intracellular mediator of ZOT-induced actin reorganization; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

REFERENCE COUNT: 12
REFERENCE(S):
(1) Anon; WO 9637196 1996 HCAPLUS
(4) Fasano; US 5665389 1997 HCAPLUS
(5) Fasano; Gastroenterology 1997, V112, P839 HCAPLUS
(6) Fasano; The Journal of Clinical Investigations 1995, V96, P710 HCAPLUS
(9) Hall; J Med Biol 1990, V211, P11 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:604931 HCAPLUS

DOCUMENT NUMBER: 129:199596
TITLE: Human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists
INVENTOR(S): Fasano, Alessio
PATENT ASSIGNEE(S): University of Maryland, Baltimore, USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9837096	A1	19980827	WO 1998-US2257	19980218
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5864014	A	19990126	US 1997-803364	19970220
US 5912323	A	19990615	US 1998-24198	19980217
AU 9862702	A1	19980909	AU 1998-62702	19980218
EP 1007553	A1	20000614	EP 1998-904957	19980218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:
US 1997-803364 A 19970220
US 1998-24198 A 19980217
WO 1998-US2257 W 19980218

AB Claimed are receptors for the zonula occludens toxin of Vibrio cholerae, including protein sequences, as well as methods involving the use of the same to screen for an agonist or antagonist of the toxin.

IC ICM C07K014-28
ICS C07K014-705; G01N033-22; G01N033-566

CC 6-3 (General Biochemistry)
Section cross-reference(s): 4, 13

IT Drug screening
Molecular association
Protein sequences
Vibrio cholerae
(human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT Protein **receptors**
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(tight junction **toxin**; human **receptor** proteins for **zonula occludens toxin** from Vibrio cholerae and use in screening for agonists and antagonists)

IT **Toxins**
RL: PRP (Properties)
(tight junction; human **receptor** proteins for **zonula**

occludens toxin from Vibrio cholerae and use in
screening for agonists and antagonists)
IT 212197-67-6 212197-68-7 212197-69-8
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; human **receptor** proteins for
zonula occludens toxin from Vibrio cholerae
and use in screening for agonists and antagonists)

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FILE 'WPIDS' ENTERED AT 08:54:30 ON 09 JUL 2001
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    SEE http://www.derwent.com/covcodes.html  <<<

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     (FILE 'WPIDS' ENTERED AT 08:51:03 ON 09 JUL 2001)
                DEL HIS Y
L1               3 S ZONULIN#
L2              15 S ZONULA OCCLUDENS (4A) TOXIN# OR ZOT
L3               2 S L2 (L) RECEPTOR#
L4               3 S L2 AND ANTAG?
L5               3 S L4 OR L3
L6               5 S L1 OR L5
L7              10 S L2 NOT L6

     FILE 'WPIDS' ENTERED AT 08:54:30 ON 09 JUL 2001

=> d .wp 1-5 16; d .wp 17 1-10


L6   ANSWER 1 OF 5  WPIDS COPYRIGHT 2001   DERWENT INFORMATION LTD
AN   2000-271257 [23]   WPIDS
DNC  C2000-082767
TI   Suppression of antigen presenting cell mediated lymphocyte proliferation,
     by administering a Zot-related immunoregulator useful for treating
     immune-related disorders, immune system rejection subsequent to tissue or
     organ transplantation.
DC   B05 D16
IN   FASANO, A; LU, R; SZTEIN, M B; TANNER, M K
PA   (UYMA-N) UNIV MARYLAND BALTIMORE
CYC  88
PI   WO 2000015252 A1 20000323 (200023)* EN   95p
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SL SZ UG ZW
         W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
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FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ
TM TR TT UA UG US UZ VN YU ZA ZW
AU 9960190 A 20000403 (200034)
NO 2001001253 A 20010315 (200134)
ADT WO 2000015252 A1 WO 1999-US18842 19990909; AU 9960190 A AU 1999-60190 19990909; NO 2001001253 A WO 1999-US18842 19990909, NO 2001-1253 20010313
FDT AU 9960190 A Based on WO 200015252
PRAI US 1998-100266 19980914
AB WO 200015252 A UPAB: 20000516
NOVELTY - A method of suppressing antigen presenting cell (APC)-mediated lymphocyte proliferation in a mammalian host pre-exposed to a particular antigen, comprising the steps of administering to the host an effective amount of a Zot-related immunoregulator selected from Zot (zonula occludens toxin) or **zonulin**, the amount effective to down-regulate the activity of the APC, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) suppressing APC-mediated lymphocyte proliferation to a particular antigen in a mammalian host comprising administering to the host an effective amount of a Zot-related immunoregulator selected from Zot or **zonulin** in combination with the particular antigen, the amount effective to down-regulate the activity of the APC;

(2) treating a mammalian host afflicted with an auto-immune or immune-related disorder or disease, comprising administering to the host an effective amount of a Zot-related immunoregulator selected from Zot or **zonulin** (optionally in combination with an antigen specific to the disease or disorder), the amount effective to down-regulate APC-mediated lymphocyte proliferation;

(3) treating a mammalian host suffering from immune system rejection subsequent to tissue or organ transplantation, comprising administering to the host an effective amount of a Zot-related immunoregulator selected from Zot or **zonulin** (optionally in combination with a specific transplantation antigen), the amount effective to down-regulate AOC-mediated lymphocyte proliferation;

(4) treating a mammalian host afflicted with inflammatory or allergic diseases or disorders, comprising administering an effective amount of a Zot-related immunoregulator selected from Zot or **zonulin** (optionally in combination with a specific inflammatory related antigen or allergen), the amount effective to down-regulate APC-mediated lymphocyte proliferation; and

(5) suppressing APC-mediated lymphocyte proliferation in a culture of cells pre-exposed to a particular antigen comprising contacting the culture with an amount of a Zot-related immunoregulator, selected from Zot or **zonulin** (optionally in combination with the antigen), the amount effective to down regulate the activity of the APC.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The method can be used to down-regulate APC-mediated lymphocyte proliferation in mammalian hosts suffering from auto-immune or

immune-related disorders, immune system rejection subsequent to tissue or organ transplantation, or inflammatory or allergic diseases. The autoimmune or immune related disorders include multiple sclerosis, rheumatoid arthritis, insulin dependent diabetes mellitus, celiac disease,
Sjogren's syndrome, systemic lupus erythematosus, auto-immune thyroiditis,
idiopathic thrombocytopenic purpura, hemolytic anemia, Grave's disease, Addison disease, autoimmune orchitis, pernicious anemia, vasculitis, autoimmune coagulopathies, myasthenia gravis, polyneuritis, pemphigus, rheumatic carditis, polymyositis, Dermatomyositis, and scleroderma. The inflammatory or allergic disease or disorder is selected from asthma, psoriasis, eczematous dermatitis, Karposi's sarcoma, multiple sclerosis, inflammatory bowel disease, proliferative disorders of smooth muscle cells, and inflammatory conditions associated with mycotic, viral, parasitic, or bacterial infections (all claimed).
ADVANTAGE - None given.
Dwg.0/13

L6 ANSWER 2 OF 5 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-205565 [18] WPIDS
DNC C2000-063366
TI New peptide **antagonist** of **zonulin** useful as antiinflammatory agent for treating cerebral ischemia, stroke, cerebral edema, gastritis, shigellosis, viral gastroenteritis, meningitis, encephalomyelitis.
DC B04 D16
IN FASANO, A
PA (UYMA-N) UNIV MARYLAND BALTIMORE
CYC 86
PI WO 2000007609 A1 20000217 (200018)* EN 69p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9954590 A 20000228 (200030)
EP 1102596 A1 20010530 (200131) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 2001000567 A 20010402 (200131)
ADT WO 2000007609 A1 WO 1999-US16683 19990728; AU 9954590 A AU 1999-54590 19990728; EP 1102596 A1 EP 1999-940809 19990728, WO 1999-US16683 19990728;
NO 2001000567 A WO 1999-US16683 19990728, NO 2001-567 20010202
FDT AU 9954590 A Based on WO 200007609; EP 1102596 A1 Based on WO 200007609
PRAI US 1998-127815 19980803
AB WO 200007609 A UPAB: 20000412
NOVELTY - A peptide **antagonist** of **zonulin** (Z) (I) comprising one of 25 amino acid sequences, all fully defined in the specification, and which binds to a **zonula occludens toxin** (**ZOT**) **receptor**, yet does not physiologically modulate the opening of mammalian tight junctions (TJ), is new.
ACTIVITY - Antiinflammatory; cerebroprotective; neuroprotective;

dermatological; antiulcer; antiviral; antibacterial; cytostatic; anti-HIV; vulnerary; antiallergic; hypotensive; immunosuppressive; antiparasitic; vasotropic.

MECHANISM OF ACTION - **Zonulin** peptide **antagonist** (claimed).

USE - (I) with a fully defined sequence of (1)-(24) is used as an antiinflammatory agent for treating gastrointestinal inflammation in which (I) binds to **ZOT receptor** in the intestine and yet does not physiologically modulate the opening of TJ in the intestine (claimed). Gastrointestinal inflammation conditions give rise to increased intestinal permeability and the peptides are useful for treating intestinal conditions that cause protein losing enteropathy caused by infection, e.g., C.difficile infection, enterocolitis, shigellosis, viral gastroenteritis, parasite infestation, bacterial overgrowth, whipple's disease, diseases with mucosal erosion or ulcerations, e.g., gastritis, gastric cancer, collagenous colitis, inflammatory bowel disease, diseases marked by lymphatic obstruction, e.g. congenital intestinal lylmphangiectasia, sarcoidosis lymphoma, mesenteric tuberculosis, and after surgical correction of congenital heart disease with Fontan's operation, mucosal diseases without ulceration, e.g., Menetrier's disease, celiac disease, eosinophilic gastroenteritis, and Immune diseases, e.g., systemic lupus erythematosus or food allergies, primarily to milk. (I) with the sequence of (35) is used for treating a condition associated with break down of blood brain barrier such as osmotic injuries, e.g., cerebral ischemia, stroke or cerebral edema, hypertension, convulsive seizure, chemical toxins, uremia, meningitis, encephalitis, encephalomyelitis, e.g., infective, or bacterial or allergic, tumors, traumatic brain injuries, radiation brain injury, immaturity and kernicterus, demyelinating diseases, e.g., multiple sclerosis or Guillian-Barre syndrome, in which (I) binds to **ZOT receptor** in the brain and yet does not physiologically modulate the opening of tight junctions in the brain (claimed). (I) is also used as an immunogen to obtain antibodies. These antibodies can be used to assay for (Z) in body tissue or fluids, in purification of (Z), or alternatively bind to (Z), and inhibiting its activity, e.g., to inhibit gastrointestinal inflammation or to inhibit breakdown of the blood brain barrier.

Dwg.0/8

L6 ANSWER 3 OF 5 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-095473 [08] WPIDS
DNC C1999-028163
TI Use of bromelain for preparation of agent for increasing absorption of macromolecular bioactive agent - allows oral dosage of insulin, glucagon, calcitonin, hGH, TSH, FSH, LH, Tpa, factor VIII, antibodies, interferon and enzymes.
DC B04 B07 D16
IN FASANO, A; MYNOTT, T L
PA (CORT-N) CORTECS UK LTD; (UYMA-N) UNIV MARYLAND BALTIMORE; (PROV-N) PROVALIS UK LTD
CYC 83
PI WO 9900141 A1 19990107 (199908)* EN 30p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG
MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG
US UZ VN YU ZW
AU 9882254 A 19990119 (199922)
EP 994720 A1 20000426 (200025) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9900141 A1 WO 1998-GB1895 19980626; AU 9882254 A AU 1998-82254
19980626; EP 994720 A1 EP 1998-932308 19980626, WO 1998-GB1895 19980626
FDT AU 9882254 A Based on WO 9900141; EP 994720 A1 Based on WO 9900141
PRAI GB 1997-13667 19970627
AB WO 9900141 A UPAB: 19990224
Use of bromelain for preparation of an agent for increasing absorption of a macromolecular bioactive agent after oral administration, is new. Also new is the use of an anti-bromelain antibody for preparation of an agent for reversing increased intestinal permeability induced by bromelain.

USE - Absorption of wide range of proteins, peptides, hormones, and enzymes and their inhibitors can be improved by the method. They include most notably insulin; also glucagon, parathyroid hormone (PTH) and its **antagonists**, calcitonin, vasopressin, renin, prolactin, growth hormone (GH), thyroid stimulating hormone (TSH), corticotropin, follicle stimulating hormone (FSH), luteinising hormone (LH), interferon, chorionic gonadotrophin, tissue plasminogen activator (Tpa), gamma globulin, blood clotting factor VIII, transferases, hydrolases, esterases, glycosidases, phosphatases, lipases, isomerisases, oxidoreductases, tumour angiogenesis factor, epidermal growth factor, nerve growth factor, insulin-like growth factors, antibodies, vaccines, and the enzyme inhibitors leupeptin, chymostatin, and pepstatin.

ADVANTAGE - Oral administration of medication is preferred by many patients to injections, increasing compliance. Bromelain is well known, and has already been in clinical use for many years as an antiinflammatory agent and for debridement of third degree burns. It has no adverse effects on nutrient influx, all suggesting safe use; in any case, any adverse effects can be rapidly and easily reversed by the antibody as described above. Bromelain is also readily available, cheap, and is a plant substance, unlike the prior art permeability increasing substance **Zot**, derived from a pathogenic organism and without means for reversal.

Dwg.0/2

L6 ANSWER 4 OF 5 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-070123 [06] WPIDS
DNC C1999-020657
TI New purified **zonulin** - which is capable of reversibly opening mammalian tight junctions, used for enhancing the delivery of agents across intestinal and nasal mucosa and blood brain barrier.
DC B04 D16
IN FASANO, A
PA (UYMA-N) UNIV MARYLAND BALTIMORE
CYC 83
PI WO 9852415 A1 19981126 (199906)* EN 63p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9872491 A 19981211 (199917)
US 5945510 A 19990831 (199942)
EP 982988 A1 20000308 (200017) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9852415 A1 WO 1998-US7636 19980428; AU 9872491 A AU 1998-72491 19980428; US 5945510 A US 1997-859931 19970521; EP 982988 A1 EP 1998-919778 19980428, WO 1998-US7636 19980428
FDT AU 9872491 A Based on WO 9852415; EP 982988 A1 Based on WO 9852415
PRAI US 1997-859931 19970521
AB WO 9852415 A UPAB: 19990210
(A) Pure **zonulin** is claimed which has an apparent mol. wt. of 47 kD, as determined by SDS-PAGE which is recognised by both anti-tau polyclonal antibody and by anti-zonula occludens toxin (ZOT) polyclonal antibody, and is capable of reversibly opening mammalian tight junctions.

USE - The **zonulin** polypeptides function as physiological modulators of mammalian tight junctions. They can be used for enhancing the absorption of therapeutic agents across tight junctions of intestinal and nasal mucosa and across tight junctions of the blood brain barrier. The **zonulin** can be used with agents such as drugs, e.g. lidocaine, adenosine, dobutamine, dopamine, epinephrine, norepinephrine, phentolamine, doxapram, alfentanil, dezocin, nalbuphine, buprenorphine, naloxone, ketorolac, midazolam, propofol, metacurine, mivacurium, succinylcholine, cytarabine, mitomycin doxorubicin, vincristine, vinblastine, methicillin, mezlocillin, piperacillin, cetoxitin, cefenicid, cefmetazole and aztreonam, a hormone e.g. testosterone, nandrolene, menotropins, insulin, urofolltropin, interferon- alpha , interferon- beta , interferon- gamma , interleukin-1 (IL-1), IL-2, IL-4, IL-8, polyvalent IgG, specific IgG, IgA, or IgM (claimed). The polypeptides can also be used for the production of antibodies which can be used to assay for **zonulin** in body tissue or fluids, or in affinity-purification of **zonulin**.
Dwg.0/6

L6 ANSWER 5 OF 5 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-467493 [40] WPIDS
DNN N1998-364271 DNC C1998-141764
TI New **zonula occludens toxin receptors** - for identifying **receptor antagonists** which can be used as anti-inflammatory drugs and agonists useful as intestinal/nasal adsorption enhancers.
DC B04 S03
IN FASANO, A
PA (UYMA-N) UNIV MARYLAND BALTIMORE
CYC 82
PI WO 9837096 A1 19980827 (199840)* EN 78p
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG

UZ VN YU ZW
AU 9862702 A 19980909 (199905)
US 5864014 A 19990126 (199911)
US 5912323 A 19990615 (199930)
US 5948629 A 19990907 (199943)
EP 1007553 A1 20000614 (200033) EN
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 9837096 A1 WO 1998-US2257 19980218; AU 9862702 A AU 1998-62702 19980218; US 5864014 A US 1997-803364 19970220; US 5912323 A CIP of US 1997-803364 19970220, US 1998-24198 19980217; US 5948629 A CIP of US 1997-803364 19970220, Div ex US 1998-24198 19980217, US 1998-186409 19981105; EP 1007553 A1 EP 1998-904957 19980218, WO 1998-US2257 19980218
FDT AU 9862702 A Based on WO 9837096; US 5948629 A CIP of US 5864014; EP 1007553 A1 Based on WO 9837096
PRAI US 1998-24198 19980217; US 1997-803364 19970220; US 1998-186409 19981105
AB WO 9837096 A UPAB: 19981008
Purified Vibrio cholera **zonula occludens toxin** (**ZOT**) **receptors**, defined as follows, are new: (a) a 45 kDa protein with N-terminal amino acid sequence (I), (II) or (III); and (b) a 66 kDa protein with the N-terminal amino acid sequence (IV).

Xaa-Leu-Thr-Glu-Leu-Glu-Lys-Ala-Leu-Asn-Xaa-Gly-Gly-Gly-Val-Gly-His-Lys-Tyr (I)

Ser-Ala-Ile-Phe-Pro-Ser-Lys-Xaa-Ser-Ala-Ser-Ile-Gly (II)

Xaa-Val-Arg-Glu-Gln-Pro-Arg-Leu-Phe-Pro-Pro-Ser-Ala-Asp-Tyr (III)

Xaa-Leu-His-Lys-Ser-Glu-Ala-Ala-His-Arg-Phe-Lys-Asp-Leu-Gln-Glu (IV)

Xaa = not defined.

Also claimed are: (1) a screening method for (ant)agonists of V. cholera **ZOT**; and (2) any resulting (ant)agonists found by the method.

USE - The **ZOT receptor** is used as capture ligand in affinity assays for agonists and **antagonists** of the toxin (claimed). **Antagonists** of **ZOT** are specifically useful as anti-inflammatory drugs in the treatment of gastrointestinal conditions that display an increased intestinal permeability, e.g. inflammatory bowel diseases, protein loosing enteropathy, food allergies, and coeliac disease. Agonists of **ZOT** can rapidly open tight junctions in a reversible and reproducible manner and are useful as intestinal or nasal adsorption enhancers. The **receptors** are also useful for generating monoclonal or polyclonal antibodies (using conventional techniques), and to purify **ZOT** and fusion proteins comprising **ZOT** by affinity chromatography.

Dwg.0/4

L7 ANSWER 1 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-505719 [45] WPIDS
DNN N2000-374010 DNC C2000-151720
TI Particle for oral administration of biopolymeric drugs, e.g. proteins or nucleic acids, comprises active ingredient in a substrate and a coating of mucoadhesive for attachment to intestinal mucosa.

DC A96 B04 B05 B07 D16 P34
IN DEHLINGER, P J; FERRARI, M; FRIEND, D R; GROVE, C F; MARTIN, F J
PA (IMED-N) IMEDD; (REGC) UNIV CALIFORNIA
CYC 21
PI WO 2000041740 A2 20000720 (200045)* EN 48p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 2000024947 A 20000801 (200054)
ADT WO 2000041740 A2 WO 2000-US362 20000107; AU 2000024947 A AU 2000-24947 20000107
FDT AU 2000024947 A Based on WO 200041740
PRAI US 1999-115424 19990111; US 1999-115420 19990111
AB WO 200041740 A UPAB: 20000918
NOVELTY - Particle (A) for oral delivery of a biopolymeric drug (I) (e.g. polypeptide, protein or nucleic acid), comprising a substrate having at least 1 reservoir containing (I) in releasable form and opening to 1 face of the substrate, which is coated with a mucoadhesive agent (II) for the attachment of (A) to the intestinal mucosa so that (I) is released directly into the lining, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an oral composition containing many (A); and

(2) a microfabrication method comprising exposing a sheet of particle-forming material to a photoablative light source through a mask, so that a network pattern corresponding to the required shape and size of (A) is produced, and continuing exposure until (A) are formed.

USE - (A) are used for the oral delivery of (I) to the intestines, e.g., the delivery of erythropoietin (for treating anemia), interferons (hepatitis), interleukins (cancer), insulin (diabetes mellitus), calcitonin (osteoporosis) and antisense oligonucleotides (cancer, infections, inflammation).

ADVANTAGE - (II) ensure attachment to the intestines and their shape, size, density and composition can be adjusted to control contact with the gut wall. (A) are too large to undergo endocytosis by gut epithelial cells and they can be labeled for detection or visualization. They may also include penetration enhancers; protease inhibitors or agents that control release rate of (I), to improve bioavailability.

Dwg.0/8

L7 ANSWER 2 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-398781 [34] WPIDS
DNC C1998-120741
TI Nasal delivery composition comprising **Zonula occludens toxin** - useful for, e.g. enhancing nasal absorption of wide variety of biologically active agents.
DC B04 B05 B07
IN DEMAGISTRIS, T; FASANO, A; RAPPUOLI, R; UZZAU, S; DE MAGISTRIS, T
PA (CHIR-N) CHIRON SPA; (UYMA-N) UNIV MARYLAND BALTIMORE
CYC 82
PI WO 9830211 A1 19980716 (199834)* EN 40p
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG

UZ VN YU ZW
AU 9859063 A 19980803 (199850)
US 5908825 A 19990601 (199929)
EP 1028715 A1 20000823 (200041) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9830211 A1 WO 1998-US19 19980109; AU 9859063 A AU 1998-59063 19980109; US 5908825 A US 1997-781057 19970109; EP 1028715 A1 EP 1998-902381 19980109, WO 1998-US19 19980109
FDT AU 9859063 A Based on WO 9830211; EP 1028715 A1 Based on WO 9830211
PRAI US 1997-781057 19970109
AB WO 9830211 A UPAB: 19980826
Composition for nasal delivery comprises: (a) a therapeutic agent, and (b)
a nasal absorption enhancing effective amount of purified Vibrio cholera **zonula occludens toxin(ZOT)**.
USE - The composition is used for the nasal delivery of therapeutic agents, e.g. biologically active peptides, vaccines, drugs that act on the
cardiovascular or central nervous systems, antineoplastics and antibiotics. The **zonula occludens toxin** is
present in the composition in an amount from about 40-1000 ng and the ratio of therapeutic agent to toxin is in the range about 1:5 to 2:1.
ADVANTAGE - The Vibrio cholera toxin acts as a nasal absorption enhancer and rapidly opens tight junctions of the nasal epithelia in a rapid and reversible manner, in a safe manner without damaging the nasal epithelium.
Dwg.1/4

L7 ANSWER 3 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1997-020921 [02] WPIDS
DNC C1997-006718
TI Oral compsn. for intestinal drug delivery - contains **zonula occludens toxin** to increase tissue permeability without damaging intestinal epithelium, esp. for insulin.
DC B04 B05 B07
IN FASANO, A
PA (UYMA-N) UNIV MARYLAND BALTIMORE
CYC 71
PI WO 9637196 A1 19961128 (199702)* EN 82p
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
AU 9657929 A 19961211 (199713)
US 5665389 A 19970909 (199742) 33p
EP 828481 A1 19980318 (199815) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 5827534 A 19981027 (199850)
AU 702385 B 19990218 (199919)
JP 11505844 W 19990525 (199931) 70p
ADT WO 9637196 A1 WO 1996-US6870 19960516; AU 9657929 A AU 1996-57929 19960516; US 5665389 A CIP of US 1995-443864 19950524, US 1996-598852 19960209; EP 828481 A1 EP 1996-914626 19960516, WO 1996-US6870 19960516; US 5827534 A US 1995-443864 19950524; AU 702385 B AU 1996-57929 19960516; JP 11505844 W JP 1996-535743 19960516, WO 1996-US6870 19960516
FDT AU 9657929 A Based on WO 9637196; EP 828481 A1 Based on WO 9637196; AU

702385 B Previous Publ. AU 9657929, Based on WO 9637196; JP 11505844 W Based on WO 9637196
PRAI US 1996-598852 19960209; US 1995-443864 19950524
AB WO 9637196 A UPAB: 19970108
Oral dosage compsn. (A) for intestinal delivery comprises an active ingredient (I) and zona occludens toxin (II) to increase intestinal absorption.

(I) are pref. cardiovascular agents (e.g. lidocaine, adenosine or epinephrine); CNS agents (e.g. doxapram, dezocin or ketorolac); antineoplastic agents (e.g. mitomycin, doxorubicin or vincristine); antibiotics (e.g. methicillin, cetoxitin or cefmetazole); hormones (e.g. testosterone, insulin or urofallotropin); lymphokines (e.g. interferons and interleukins); Ig (e.g. polyvalent IgG or specific IgG, IgA or IgM) or albumin. Also suitable are peptide antigens and attenuated microbial vaccines.

USE - (A) is used to deliver drugs, peptides and vaccines, specifically insulin.

ADVANTAGE - (II), a product of Vibrio cholerae, induces a rapid, reversible and reproducible opening of the tight junctions in the intestines, increasing tissue permeability. It can be used without damaging the intestinal epithelium and allows oral admin. of (I) that can not otherwise be absorbed by transcellular pathways, regardless of their size or charge. When insulin is admin. with (II), no severe hypo- or hyper-glycaemia is induced, even at doses at most 20 times the usual parenteral dose.
Dwg.0/10

L7 ANSWER 4 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-412060 [41] WPIDS
DNN N1996-346898 DNC C1996-129846
TI Detection of bacterial virulence-associated factor in faeces - by immunoassay after release with soln. contg. surfactant, urea and antibiotic.
DC A96 B04 D16 S03
IN THORNE, G M
PA (CHIL-N) CHILDRENS MEDICAL CENT
CYC 1
PI US 5552294 A 19960903 (199641)* 9p
ADT US 5552294 A Cont of US 1992-963724 19921020, US 1994-279832 19940725
PRAI US 1992-963724 19921020; US 1994-279832 19940725
AB US 5552294 A UPAB: 19961011
Method for detecting a virulence-associated factor (VAF) in a faecal sample comprises:

(a) treating the sample with a VAF-releasing soln. to release 1 VAF from any VAF-producing bacteria in the sample and

(b) immunochemically detecting the presence or amt. of released VAF.

The VAF is a bacterial toxin, surface antigen, adhesive factor or heat-release protein. The VAF-releasing soln. contains a surfactant, urea and an antibiotic selected from polymyxins and mitomycin C.

USE - The method is used esp. for detecting Shiga-like toxin I (SLT I) and/or Shiga-like toxin II (SLT II), heat-labile enterotoxin, heat stabile enterotoxins a+b, heat-stabile-like enterotoxins, adhesins, lipopolysaccharide-0157 antigen, haemolysin, cholera toxin, flagella, **zot** toxin, toxin A, toxin B, surface antigen for invasion, cytotoxins, proteases, siderophores, invasins, outer membrane protein,

pili and lipopolysaccharides (all claimed).
ADVANTAGE - Bacterial toxins are released without destroying their structure and without interfering with the immunoassay.
Dwg.0/3

L7 ANSWER 5 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-322042 [32] WPIDS
DNN N1996-270958
TI Television receiver with surface acoustic wave filter coupling - has resistor coupled between two input terminals of surface acoustic wave filter to reduce signal distortion.
DC U25 V06 W03
IN RUTTEN, P J H; STIKVOORT, E F
PA (PHIG) PHILIPS ELECTRONICS NV; (PHIG) US PHILIPS CORP; (PHIG) PHILIPS NORDEN AB
CYC 20
PI WO 9620530 A1 19960704 (199632)* EN 25p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CN JP KR
EP 746904 A1 19961211 (199703) EN 1p
R: DE FR GB IT
US 5649313 A 19970715 (199734) 16p
JP 09509816 W 19970930 (199749) 29p
KR 97701448 A 19970317 (199813)
CN 1145145 A 19970312 (200103)
ADT WO 9620530 A1 WO 1995-IB1032 19951121; EP 746904 A1 EP 1995-936067 19951121, WO 1995-IB1032 19951121; US 5649313 A US 1995-574799 19951219; JP 09509816 W WO 1995-IB1032 19951121, JP 1996-520316 19951121; KR 97701448 A WO 1995-IB1032 19951121, KR 1996-704624 19960823; CN 1145145 A CN 1995-192376 19951121
FDT EP 746904 A1 Based on WO 9620530; JP 09509816 W Based on WO 9620530; KR 97701448 A Based on WO 9620530
PRAI EP 1994-203747 19941223
AB WO 9620530 A UPAB: 19960819
The receiver comprises a tuner (TUN) for converting a reception signal into an intermediate frequency (IF) signal, and a filter arrangement (FAR)
for filtering the IF signal to obtain a filtered IF signal. A demodulation
section (IFD) provides a baseband signal in response to the filtered IF signal. The filter arrangement comprises a surface acoustic wave filter (FSAW) with two input terminals (IS1,IS2) and an inductor coupled between the two input terminals. A series resonance network (SRC) is coupled to transfer the IF signal to at least one of the two input terminals.
The receiver further includes a resistor (RP) coupled between the two
input terminals of the SAW filter. Alternatively, a resistor (RS) is coupled in parallel to the series resonance network. A combination of both
measures is also possible, that is, a resistor in parallel with the input terminals and a further resistor in parallel with the resonance circuit. Pref. the tuner has an output for providing the IF signal (Vot), the output having an impedance (**Zot**) which is a magnitude lower than the value of resistor (RS) in parallel to the series resonance network.
ADVANTAGE - Performs better. Resistors do not affect noise figure and
insertion loss within pass band.

Dwg.5/13

L7 ANSWER 6 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-019870 [02] WPIDS
CR 1995-161574 [21]
DNC C1996-006821
TI New avirulent Vibrio cholerae strains - comprise deletions in the cholera **toxin** and **zonula occludens toxin** genes, for vaccination against cholera.
DC B04 D16
IN BAUDRY-MAURELLI, B; FASANO, A; KAPER, J B
PA (UYMA-N) UNIV MARYLAND BALTIMORE
CYC 1
PI US 5470729 A 19951128 (199602)* EN 55p
ADT US 5470729 A CIP of US 1983-472276 19830304, CIP of US 1984-581406 19840217, Cont of US 1986-867633 19860527, CIP of US 1989-363383 19890605, Cont of US 1990-533315 19900605, CIP of US 1992-821872 19920116, US 1992-931943 19920812
FDT US 5470729 A CIP of US 4935364, CIP of US 5135862
PRAI US 1992-931943 19920812; US 1983-472276 19830304; US 1984-581406 19840217; US 1986-867633 19860527; US 1989-363383 19890605; US 1990-533315 19900605; US 1992-821872 19920116
AB US 5470729 A UPAB: 19990511
(A) A novel culture of Vibrio cholerae (VC) comprises a strain of the Ogawa or Inaba serotype having the chromosomal DNA coding for the A subunit and B subunit of VC toxin deleted from the toxin locus to confer avirulence and retaining the capacity to colonise the intestine of a host animal, and having a second DNA fragment coding for **zonula occludens** (ZO) **toxin** deleted.
USE - The VC strains are useful for vaccination against cholera.
ADVANTAGE - The VC strains can confer 100% efficacy in humans against subsequent disease with a strain of a similar serotype while avoiding undesirable side effects such as diarrhoea, nausea, and cramping.
Dwg.0/24

L7 ANSWER 7 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1995-161574 [21] WPIDS
CR 1984-232592 [38]; 1992-007465 [01]; 1994-036582 [05]; 1995-130687 [17]; 1996-019870 [02]; 1997-280239 [25]
DNC C1995-074827
TI New avirulent strains of Vibrio cholerae expressing toxin B sub unit - are stable against reversion and useful in oral vaccines to induce local protective immunity.
DC B04 D16
IN KAPER, J B; LEVINE, M M
PA (UYMA-N) UNIV MARYLAND BALTIMORE; (UYMA-N) UNIV MARYLAND; (UYMA-N) UNIV MARYLAND SYSTEM
CYC 24
PI WO 9510300 A1 19950420 (199521)* EN 109p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA CN JP KR RU US
AU 9479714 A 19950504 (199536)
EP 722339 A1 19960724 (199634) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

JP 09504430 W 19970506 (199728) 143p
AU 699912 B 19981217 (199911)
US 5882653 A 19990316 (199918)
RU 2140981 C1 19991110 (200040)
CN 1142774 A 19970212 (200050)
ADT WO 9510300 A1 WO 1994-US11424 19941007; AU 9479714 A AU 1994-79714 19941007; EP 722339 A1 EP 1994-930665 19941007, WO 1994-US11424 19941007; JP 09504430 W WO 1994-US11424 19941007, JP 1995-511944 19941007; AU 699912 B AU 1994-79714 19941007; US 5882653 A CIP of US 1983-472276 19830304, CIP of US 1984-581406 19840217, Cont of US 1986-867633 19860527, CIP of US 1989-363383 19890605, Cont of US 1990-533315 19900605, CIP of US 1992-821872 19920116, CIP of US 1992-931943 19920812, CIP of US 1993-133438 19931008, CIP of US 1993-133439 19931008, WO 1994-US11424 19941007, US 1996-624601 19960729; RU 2140981 C1 WO 1994-US11424 19941007, RU 1996-108963 19941007; CN 1142774 A CN 1994-194095 19941007
FDT AU 9479714 A Based on WO 9510300; EP 722339 A1 Based on WO 9510300; JP 09504430 W Based on WO 9510300; AU 699912 B Previous Publ. AU 9479714, Based on WO 9510300; US 5882653 A CIP of US 4935364, CIP of US 5135862, CIP of US 5470729, Based on WO 9510300; RU 2140981 C1 Based on WO 9510300
PRAI US 1993-133439 19931008; US 1993-133438 19931008; US 1983-472276 19830304; US 1984-581406 19840217; US 1986-867633 19860527; US 1989-363383 19890605; US 1990-533315 19900605; US 1992-821872 19920116; US 1992-931943 19920812; US 1996-624601 19960729
AB WO 9510300 A UPAB: 20001010
New avirulent Vibrio cholerae strain of a non-01 serogroup has (1) DNA encoding the cholera toxin (CT) core and RS1 sequences of the CT locus deleted, and (2) DNA encoding mercury resistance and DNA encoding the CT B subunit, or part of it sufficient to confer immunogenicity, reinserted into the genome. Also new are (1) similar strains additionally having a deletion in the recA gene sufficient to render the gene non-functional in homologous recombination; (2) avirulent V. cholerae of 01 serogroup of genotype ctxA-, **zot**-, ace-, mer, ctxB; specifically strain CVD111.

USE - The new strains are used in vaccines to protect against cholera caused by non-01 strains, opt. together with CVD111 (that protects against 01 strains).

ADVANTAGE - Expression of the B subunit ensures that the new strains are immunogenic, inducing a strong local immunity when they colonise the small intestine. The mercury resistance gene allows the vaccine strain to be identified without use of antibiotics. The new strains do not revert to the CT-positive phenotype.

Dwg.25/29

L7 ANSWER 8 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1993-290094 [37] WPIDS
DNN N1993-223117
TI Focus adjusting device for inner focus lens assembly with compensator lens - includes drivers for zoom and focus lenses. Focal condition detector and

computer for determining optical end of focus lens.
DC P81 W04
IN FUJIKAWA, T; KOYANAGI, M; TAKAHASHI, H
PA (SONY) SONY CORP
CYC 6
PI EP 560646 A1 19930915 (199337)* EN 13p
R: DE FR GB
JP 05232367 A 19930910 (199341)
US 5352882 A 19941004 (199439) 13p
EP 560646 B1 19970903 (199740) EN 15p
R: DE FR GB
DE 69313489 E 19971009 (199746)
KR 256111 B1 20000501 (200128)
ADT EP 560646 A1 EP 1993-400490 19930225; JP 05232367 A JP 1992-73473 19920225; US 5352882 A US 1993-19901 19930219; EP 560646 B1 EP 1993-400490 19930225; DE 69313489 E DE 1993-613489 19930225, EP 1993-400490 19930225; KR 256111 B1 KR 1993-679 19930120
FDT DE 69313489 E Based on EP 560646
PRAI JP 1992-73473 19920225
AB EP 560646 A UPAB: 19931123
The device comprises a drive element (7) for driving a zoom lens (3) and a zoom lens position detector (12) for detecting information on the position of the zoom lens (3). A focus lens driver (8) drives a focus lens (5). A focal condition is detected (19,20).
A computer (10) calculates an optical end of the focus lens using information obtained previously on a ratio between the distance from one to the other of opposite mechanical ends of the zoom lens and the distance from one to the other of opposite optical ends of the zoom lens (3).
USE/ADVANTAGE - Facilitates flange back adjustment in video cameras and readily detects actual wide end position.
15
Dwg.4/8

L7 ANSWER 9 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1992-007465 [01] WPIDS
CR 1984-232592 [38]; 1994-036582 [05]; 1995-130687 [17]; 1995-161574 [21]; 1996-019870 [02]; 1997-280239 [25]
DNC C1992-003248
TI New Vibrio cholerae strains - comprise restriction endonuclease fragment encoding toxin, used as vaccines against cholera.
DC B04 D16
IN BAUDRY-MAURELLI, B; FASANO, A; KAPER, J B; BAUDRYMAUR, B
PA (UYMA-N) UNIV MARYLAND BALTIMORE; (UYMA-N) UNIV OF MARYLAND; (UYMA-N) UNIV MARYLAND BALTI
CYC 20
PI WO 9118979 A 19911212 (199201)* 83p
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: AU CA JP US
AU 9182147 A 19911231 (199215)
ZA 9104286 A 19920325 (199218) 82p
EP 485591 A1 19920520 (199221) EN 83p
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE

JP 05502381 W 19930428 (199322) 20p
AU 656730 B 19950216 (199515)
EP 485591 A4 19930714 (199527)
EP 485591 B1 19961106 (199649) EN 61p
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69123027 E 19961212 (199704)
ES 2095322 T3 19970216 (199714)
CA 2064046 C 19990413 (199933)
RU 2130970 C1 19990527 (200027)

ADT ZA 9104286 A ZA 1991-4286 19910605; EP 485591 A1 EP 1991-912336 19910605, WO 1991-US3812 19910605; JP 05502381 W JP 1991-511737 19910605, WO 1991-US3812 19910605; AU 656730 B AU 1991-82147 19910605; EP 485591 A4 EP 1991-912336 ; EP 485591 B1 EP 1991-912336 19910605, WO 1991-US3812 19910605; DE 69123027 E DE 1991-623027 19910605, EP 1991-912336 19910605, WO 1991-US3812 19910605; ES 2095322 T3 EP 1991-912336 19910605; CA 2064046 C CA 1991-2064046 19910605; RU 2130970 C1 SU 1991-5011181 19910605, WO 1991-US3812 19910605

FDT EP 485591 A1 Based on WO 9118979; JP 05502381 W Based on WO 9118979; AU 656730 B Previous Publ. AU 9182147, Based on WO 9118979; EP 485591 B1 Based on WO 9118979; DE 69123027 E Based on EP 485591, Based on WO 9118979; ES 2095322 T3 Based on EP 485591; RU 2130970 C1 Based on WO 9118979

PRAI US 1990-533315 19900605

AB WO 9118979 A UPAB: 20000606
The following are new: (1) a culture of Vibrio cholerae (V.c.) strain of the Ogawa or Inaba serotype having (i) first restriction endonuclease (RE) fragment of DNA encoding V.c. toxin or the A1 subunit of it pref. of the ctx gene, deleted to confer avirulence and retaining capacity to colonise the intestine of a host animal and (ii) a second RE fragment of DNA encloding **zonula occludens toxin** (**ZOT**) or fragments of it deleted to reduce residual side effects in the host.

(2) A culture of V.c. of the Ogawa or Inaba serotype having a region of the chromosomal DNA encoding cholera toxin and **ZOT** deleted to confer avivulence and retain capacity to colonise the intestine of a host animal and to reduce residual effects; and (3) methods for isolating the deletion mutants of V.c.

USE/ADVANTAGE - The V.c. strains are capable to confer 100% efficacy in protecting humans against subsequent infection with a strain of a similar serotype and avoid undesirable side effects such as diarrhoea and nanfea, and cramping. The cultures are used for prodn. of vaccines against cholera.

Dwg.0/21

L7 ANSWER 10 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1976-F8791X [26] WPIDS
TI Rocket motor injector explosion energy absorber - has viscoelastic material between complementary free piston and housing faces.
DC Q53
PA (THIO) THIOKOL CHEM CORP
CYC 1
PI US 3962862 A 19760615 (197626)*
PRAI US 1968-730744 19680521

AB US 3962862 A UPAB: 19930901
The rocket motor oxidizer injector has a housing and a passage for pressurized oxidizer through the housing. A free piston is slidable in the housing and exposed to the oxidizer passage, a viscoelastic material being interposed between the piston and the housing. The piston face adjacent the viscoelastic material is shaped to a predetermined contour and its counterpart face on the housing is of the same contour, the viscoelastic material being bonced between concentric metal rings in alternate layers with the rings parallel to the central axis of the piston. The arrangement reduces the effect of the so called **ZOT** expansions which occur in injectors of this type.

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=> d his

     (FILE 'WPIDS' ENTERED AT 08:54:30 ON 09 JUL 2001)
               DEL HIS Y

     FILE 'MEDLINE, BIOSIS' ENTERED AT 08:56:03 ON 09 JUL 2001
L1            19 S ZONULIN#
L2             0 S ZONULA OCCULDENS (L) TOXIN#
L3           114 S ZONULA OCCLUDENS (L) TOXIN#
L4            19 S L3 (L) RECEPTOR#
L5        602835 S ANTAGONI?
L6             1 S L3 AND L5
L7            19 S L6 OR L4
L8            17 DUP REM L1 (2 DUPLICATES REMOVED)
L9            13 DUP REM L7 (6 DUPLICATES REMOVED)
L10           11 S L9 NOT L8

=> d bib ab it l8 1-17;d bib ab it l10 1-11


L8   ANSWER 1 OF 17  MEDLINE
AN   2000259114      MEDLINE
DN   20259114   PubMed ID: 10801176
TI   Zonulin, a newly discovered modulator of intestinal
     permeability, and its expression in coeliac disease.
AU   Fasano A; Not T; Wang W; Uzzau S; Berti I; Tommasini A; Goldblum S E
NC   DK-48373 (NIDDK)
SO   LANCET, (2000 Apr 29) 355 (9214) 1518-9.
     Journal code: L0S; 2985213R. ISSN: 0140-6736.
CY   ENGLAND: United Kingdom
DT   Letter
LA   English
FS   Abridged Index Medicus Journals; Priority Journals
EM   200005
ED   Entered STN: 20000606
     Last Updated on STN: 20000606
     Entered Medline: 20000522
AB   We identified zonulin, a novel human protein analogue to the
     Vibrio cholerae derived Zonula occludens toxin, which induces tight
     junction disassembly and a subsequent increase in intestinal permeability
     in non-human primate intestinal epithelia. Zonulin expression
     was raised in intestinal tissues during the acute phase of coeliac
     disease, a clinical condition in which tight junctions are opened and
     permeability is increased.

L8   ANSWER 2 OF 17  BIOSIS  COPYRIGHT 2001 BIOSIS
AN   2001:164100  BIOSIS
DN   PREV200100164100
TI   Regulation of intercellular tight junctions by zonula occludens toxin and
     its eukaryotic analogue zonulin.
AU   Fasano, Alessio (1)
CS   (1) Division of Pediatric Gastroenterology and Nutrition, University of
     Maryland School of Medicine, 685 W. Baltimore St., HSF Building, Room
465,
     Baltimore, MD, 21201: afasano@umaryland.edu USA
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SO Schulzke, Joerg-Dieter; Fromm, Michael; Riecken, Ernst-Otto; Binder, Henry
J.. Annals of the New York Academy of Sciences, (December, 2000) Vol. 915,
pp. 214-222. Annals of the New York Academy of Sciences. Epithelial transport and barrier function: Pathomechanisms in gastrointestinal disorders. print.
Publisher: New York Academy of Sciences 2 East 63rd Street, New York, NY, 10021, USA.
Meeting Info.: Epithelial Transport and Barrier Function: Pathomechanisms in Gastrointestinal Disorders Berlin, Germany March 26-27, 1999
ISSN: 0077-8923. ISBN: 1-57331-259-2 (cloth), 1-57331-260-6 (paper).
DT Book; Conference
LA English
SL English
IT Major Concepts
Membranes (Cell Biology); Toxicology
IT Parts, Structures, & Systems of Organisms
intestinal epithelium: digestive system, permeability; tight junctions:
dynamic structure, intracellular, regulation
IT Chemicals & Biochemicals
PKC [protein kinase C]: activation; phorbol esters: PKC activation; zonula occludens toxin: PKC activation, toxin; **zonulin**: intercellular tight junction regulation, zonula occludens toxin analogue
IT Miscellaneous Descriptors
Book Chapter; Meeting Paper
RN 141436-78-4 (PROTEIN KINASE C)

L8 ANSWER 3 OF 17 MEDLINE DUPLICATE 1
AN 2001154383 MEDLINE
DN 20534864 PubMed ID: 11082037
TI Human **zonulin**, a potential modulator of intestinal tight junctions.
AU Wang W; Uzzau S; Goldblum S E; Fasano A
CS Division of Pediatric Gastroenterology and Nutrition, Gastrointestinal Pathophysiology Section, Center for Vaccine Development, Baltimore, MD 21201, USA.
NC DK-48373 (NIDDK)
HL-63217 (NHLBI)
SO JOURNAL OF CELL SCIENCE, (2000 Dec) 113 Pt 24 4435-40.
Journal code: HNK; 0052457. ISSN: 0021-9533.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered PubMed: 20010129
Entered Medline: 20010322
AB Intercellular tight junctions are dynamic structures involved in vectorial
transport of water and electrolytes across the intestinal epithelium. Zonula occludens toxin derived from Vibrio cholerae interacts with a specific intestinal epithelial surface receptor, with subsequent

activation of a complex intracellular cascade of events that regulate tight junction permeability. We postulated that this toxin may mimic the effect of a functionally and immunologically related endogenous modulator of intestinal tight junctions. Affinity-purified anti-zonula occludens toxin antibodies and the Ussing chamber assay were used to screen for one or more mammalian zonula occludens toxin analogues in both fetal and adult human intestine. A novel protein, **zonulin**, was identified that induces tight junction disassembly in non-human primate intestinal epithelia mounted in Ussing chambers. Comparison of amino acids in the active zonula occludens toxin fragment and **zonulin** permitted the identification of the putative receptor binding domain within the N-terminal region of the two proteins. **Zonulin** likely plays a pivotal role in tight junction regulation during developmental, physiological, and pathological processes, including tissue morphogenesis, movement of fluid, macromolecules and leukocytes between the intestinal lumen and the interstitium, and inflammatory/autoimmune disorders.

L8 ANSWER 4 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:222555 BIOSIS
DN PREV200100222555
TI **Zonulin**, a newly discovered modulator of intestinal permeability, and its expression in coeliac disease.
AU Fasano, Alessio (1); Not, Tarcisio; Wang, Wenle; Uzzau, Sergio; Berti, Irene; Tommasini, Alberto; Goldblum, Simeon E.
CS (1) Division of Paediatric Gastroenterology and Nutrition, and Gastrointestinal Pathophysiology Section, Center for Vaccine Development, School of Medicine, University of Maryland, Baltimore, MD, 21201: afasano@umaryland.edu USA
SO Lancet (North American Edition), (29 April, 2000) Vol. 355, No. 9214, pp. 1518-1519. print.
ISSN: 0099-5355.
DT Article
LA English
SL English
AB We identified **zonulin**, a novel human protein analogue to the Vibrio cholerae derived Zonula occludens toxin, which induces tight junction disassembly and a subsequent increase in intestinal permeability in non-human primate intestinal epithelia. **Zonulin** expression was raised in intestinal tissues during the acute phase of coeliac disease, a clinical condition in which tight junctions are opened and permeability is increased.
IT Major Concepts
Digestive System (Ingestion and Assimilation)
IT Parts, Structures, & Systems of Organisms
intestinal epithelium: digestive system; intestine: digestive system, permeability; small intestinal tight junction: digestive system
IT Diseases
celiac disease: digestive system disease, metabolic disease
IT Chemicals & Biochemicals
zonula occludens toxin [ZOT]; **zonulin**: expression
IT Alternate Indexing
Celiac Disease (MeSH)
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Vibrionaceae: Facultatively Anaerobic Gram-Negative Rods, Eubacteria,

Bacteria, Microorganisms
ORGN Organism Name
Vibrio cholerae (Vibrionaceae); human (Hominidae): patient
ORGN Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Humans; Mammals; Microorganisms; Primates; Vertebrates

L8 ANSWER 5 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:515072 BIOSIS
DN PREV200000515072
TI Alterations in **zonulin** secretion accompany the increase in permeability in BB/wor diabetic rats.
AU Watts, T.; Berti, I. (1); Not, T. (1); Tommasini, A. (1); Panfili, E. (1);
Santon, D. (1); Soban, M.; El Asmar, R.; Di Pierro, M.; Margaretten, K.; Fasano, A.
CS (1) Department of Paediatrics, IRCCS Burlo Garofolo, Trieste Italy
SO Scandinavian Journal of Immunology, (October, 2000) Vol. 52, No. 4, pp. 423. print.
Meeting Info.: 2nd European Mucosal Immunity Group Meeting Gothenburg, Sweden October 06-08, 2000
ISSN: 0300-9475.
DT Conference
LA English
SL English
IT Major Concepts
Endocrine System (Chemical Coordination and Homeostasis); Digestive System (Ingestion and Assimilation)
IT Parts, Structures, & Systems of Organisms
cecum: digestive system; ileum: digestive system; jejunum: digestive system
IT Diseases
diabetes: endocrine disease/pancreas, metabolic disease
IT Chemicals & Biochemicals
zonulin: secretion
IT Alternate Indexing
Diabetes Mellitus (MeSH)
IT Miscellaneous Descriptors
intestinal permeability; Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae): BB/wor, animal model, male, white
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L8 ANSWER 6 OF 17 MEDLINE DUPLICATE 2
AN 2000083425 MEDLINE
DN 20083425 PubMed ID: 10617135
TI Affinity purification and partial characterization of the **zonulin** /zonula occludens toxin (Zot) receptor from human brain.
AU Lu R; Wang W; Uzzau S; Vigorito R; Zielke H R; Fasano A
CS Division of Pediatric Gastroenterology and Nutrition and Center for Vaccine Development, University of Maryland School of Medicine, Baltimore 21201, USA.
NC AI-35740 (NIAID)

DK-48373 (NIDDK)
SO JOURNAL OF NEUROCHEMISTRY, (2000 Jan) 74 (1) 320-6.
Journal code: JAV; 2985190R. ISSN: 0022-3042.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200001
ED Entered STN: 20000131
Last Updated on STN: 20000131
Entered Medline: 20000118
AB The intercellular tight junctions (TJs) of endothelial cells represent the limiting structure for the permeability of the blood-brain barrier (BBB). Although the BBB has been recognized as being the interface between the bloodstream and the brain, little is known about its regulation. **Zonulin** and its prokaryotic analogue, zonula occludens toxin (Zot) elaborated by Vibrio cholerae, both modulate intercellular TJs by binding to a specific surface receptor with subsequent activation of an intracellular signaling pathway involving phospholipase C and protein kinase C activation and actin polymerization. Affinity column purification revealed that human brain plasma membrane preparations contain two Zot binding proteins of approximately 55 and approximately 45 kDa. Structural and kinetic studies, including saturation and competitive assays, identified the 55-kDa protein as tubulin, whereas the 45-kDa protein represents the **zonulin**/Zot receptor. Biochemical characterization provided evidence that this receptor is a glycoprotein containing multiple sialic acid residues. Comparison of the N-terminal sequence of the **zonulin**/Zot receptor with other protein sequences by BLAST analysis revealed a striking similarity with MRP-8, a 14-kDa member of the S-100 family of calcium binding proteins. The discovery and characterization of this receptor from human brain may significantly contribute to our knowledge on the pathophysiological regulation of the BBB.

L8 ANSWER 7 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:536317 BIOSIS
DN PREV200000536317
TI **Zonulin** in the impairment of the gut barrier function following small intestinal bacterial colonization.
AU El Asmar, Ramzi (1); Panighrai, Pinaki; Bamford, Penny; Berti, Irene; Not, Tarcisio; Catassi, Carlo; Coppa, Giovanni; Fasano, Alessio
CS (1) Pediatrics Gastroenterology and Nutrition, University of Maryland, Baltimore, MD USA
SO JPGN, (2000) Vol. 31, No. Supplement 2, pp. S279. print.
Meeting Info.: World Congress of Pediatric Gastroenterology, Hepatology, and Nutrition Boston, Massachusetts, USA August 05-09, 2000
DT Conference
LA English
SL English
IT Major Concepts
Biochemistry and Molecular Biophysics; Infection; Digestive System (Ingestion and Assimilation); Gastroenterology (Human Medicine, Medical Sciences)

IT Parts, Structures, & Systems of Organisms
gut: barrier function, digestive system; small intestine: cultured, digestive system, permeability
IT Chemicals & Biochemicals
zonulin: intestinal concentration, secretion
IT Methods & Equipment
Western immunoblotting: analytical method; sandwich-ELISA: analytical method
IT Miscellaneous Descriptors
transepithelial electrical resistance; Meeting Abstract
ORGN Super Taxa
Bacteria: Microorganisms; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Leporidae: Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Primates: Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
bacteria (Bacteria): intestinal colonization, pathogen; human (Hominidae); monkey (Primates): animal model; rabbit (Leporidae): animal model; rat (Muridae): animal model
ORGN Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Humans; Lagomorphs; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Primates; Nonhuman Vertebrates; Primates; Rodents; Vertebrates

L8 ANSWER 8 OF 17 MEDLINE
AN 2001100020 MEDLINE
DN 21035451 PubMed ID: 11193578
TI Regulation of intercellular tight junctions by zonula occludens toxin and its eukaryotic analogue **zonulin**.
AU Fasano A
CS Division of Pediatric Gastroenterology and Nutrition, Gastrointestinal Pathophysiology Section, Center for Vaccine Development, Department of Physiology, University of Maryland School of Medicine, Baltimore, MD 21201, USA.. afasano@umaryland.edu
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (2000) 915 214-22. Ref: 60
Journal code: 5NM. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals
EM 200102
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20010118
Entered Medline: 20010201
AB The intestinal epithelium represents the largest interface between the external environment and the internal host milieu and constitutes the major barrier through which molecules can either be absorbed or secreted. There is now substantial evidence that tight junctions (tj) play a major role in regulating epithelial permeability by influencing paracellular flow of fluid and solutes. Tj are one of the hallmarks of absorptive and secretory epithelia. Evidence now exists that tj are dynamic rather than static structures and readily adapt to a variety of developmental, physiological, and pathological circumstances. These adaptive mechanisms are still incompletely understood. Activation of PKC either by Zonula

occludens toxin (Zot) or by phorbol esters increases paracellular permeability. Alteration of epithelial tj is a recently described property for infectious agents. Clostridium difficile toxin A and B and influenza and vesicular stomatitis viruses have been shown to loosen tj in tissue culture monolayers. Unlike what occurs after the Zot stimulus, these changes appear to be irreversible and are associated with destruction of the tj complex. On the basis of this observation, we postulated that Zot may mimic the effect of a functionally and immunologically related endogenous modulator of epithelial tj. We were able to identify an intestinal Zot analogue, which we named **zonulin**. It is conceivable that the **zonulins** participate in the physiological regulation of intercellular tj not only in the small intestine, but also throughout a wide range of extraintestinal epithelia as well as the ubiquitous vascular endothelium, including the blood-brain barrier. Disregulation of this hypothetical **zonulin** model may contribute to disease states that involve disordered intercellular communication, including developmental and intestinal disorders, tissue inflammation, malignant transformation, and metastasis.

L8 ANSWER 9 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:193618 BIOSIS
DN PREV200000193618
TI Probiotics prevent **zonulin**-mediated intestinal barrier dysfunction secondary to bacterial colonization.
AU El Asmar, R. (1); Fasano, A.; Bamford, P.; Berti, I.; Not, T.; Catassi, C.; Coppa, G. V.; Panigrahi, P.
CS (1) Pediatrics, University of Maryland, Baltimore, MD USA
SO Pediatric Research, (April, 2000) Vol. 47, No. 4 Part 2, pp. 163A. Meeting Info.: Joint Meeting of the Pediatric Academic Societies and the American Academy of Pediatrics. Boston, Massachusetts, USA May 12-16, 2000
American Academy of Pediatrics
. ISSN: 0031-3998.
DT Conference
LA English
SL English
IT Major Concepts
Digestive System (Ingestion and Assimilation)
IT Parts, Structures, & Systems of Organisms
gut mucosa: barrier function, digestive system, permeability, transcytosis; intestine: digestive system; small intestine: digestive system
IT Chemicals & Biochemicals
inulin: transport; **zonulin**: release
IT Miscellaneous Descriptors
bacterial colonization; transepithelial electrical resistance; Meeting Abstract; Meeting Poster
ORGN Super Taxa
Cercopithecidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Enterobacteriaceae: Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms; Leporidae: Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia; Regular Nonsporing Gram-Positive Rods: Eubacteria, Bacteria, Microorganisms
ORGN Organism Name
E.coli [Escherichia coli] (Enterobacteriaceae); Lactobacillus plantarum

(Regular Nonsporing Gram-Positive Rods): probiotic, strain-PP-217; rabbit (Leporidae); rhesus monkey (Cercopithecidae)
ORGN Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Lagomorphs; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Primates; Nonhuman Vertebrates; Primates; Vertebrates
RN 9005-80-5 (INULIN)

L8 ANSWER 10 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:193619 BIOSIS
DN PREV200000193619
TI **Zonulin** is involved in the impairment of the gut barrier function following small intestinal bacterial colonization.
AU El Asmar, R. (1); Panigrahi, P.; Bamford, P.; Berti, I.; Not, T.; Catassi, C.; Coppa, G. V.; Fasano, A.
CS (1) Pediatrics Dept, University of Maryland, Baltimore, MD USA
SO Pediatric Research, (April, 2000) Vol. 47, No. 4 Part 2, pp. 163A. Meeting Info.: Joint Meeting of the Pediatric Academic Societies and the American Academy of Pediatrics. Boston, Massachusetts, USA May 12-16, 2000
American Academy of Pediatrics
. ISSN: 0031-3998.
DT Conference
LA English
SL English
IT Major Concepts
Membranes (Cell Biology); Digestive System (Ingestion and Assimilation)
IT Parts, Structures, & Systems of Organisms
intestine: digestive system, permeability
IT Chemicals & Biochemicals
inulin: transport; **zonulin**: secretion
IT Miscellaneous Descriptors
transepithelial electrical resistance; Meeting Abstract; Meeting Poster
ORGN Super Taxa
Leporidae: Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Primates: Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
monkey (Primates); rabbit (Leporidae); rat (Muridae)
ORGN Organism Superterms
Animals; Chordates; Lagomorphs; Mammals; Nonhuman Mammals; Nonhuman Primates; Nonhuman Vertebrates; Primates; Rodents; Vertebrates
RN 9005-80-5 (INULIN)

L8 ANSWER 11 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:268201 BIOSIS
DN PREV200000268201
TI Probiotics prevent **zonulin**-mediated intestinal barrier dysfunction secondary to bacterial colonization.
AU El Asmar, Ramzi (1); Fasano, Alessio; Bamford, Penelope; Berti, Irene; Not, Tarcisio; Catassi, Carlo; Coppa, Giovanni V.; Panigrahi, Pinaki
CS (1) Univ of Maryland, Baltimore, MD USA
SO Gastroenterology, (April, 2000) Vol. 118, No. 4 Suppl. 2 Part 1, pp. AGA A815. print..

Meeting Info.: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week. San Diego, California, USA May
21-24, 2000 American Gastroenterological Association
. ISSN: 0016-5085.
DT Conference
LA English
SL English
IT Major Concepts
Infection; Digestive System (Ingestion and Assimilation)
IT Parts, Structures, & Systems of Organisms
gut mucosa: digestive system
IT Chemicals & Biochemicals
probiotics
IT Miscellaneous Descriptors
bacterial colonization; **zonulin**-mediated intestinal barrier dysfunction; Meeting Abstract
ORGN Super Taxa
Leporidae: Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia; Regular Nonsporing Gram-Positive Rods: Eubacteria, Bacteria, Microorganisms
ORGN Organism Name
Lactobacillus plantarum (Regular Nonsporing Gram-Positive Rods): pathogen, strain-PP-217; rabbit (Leporidae)
ORGN Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Lagomorphs; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Vertebrates

L8 ANSWER 12 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:268595 BIOSIS
DN PREV200000268595
TI **Zonulin** is involved in the impairment of the gut barrier function following small intestinal bacterial colonization.
AU El Asmar, Ramzi (1); Paningrahi, Pinaki; Bamford, Penelope; Berti, Irene; Not, Tarcisio; Catassi, Carlo; Coppa, Giovanni V.; Fasano, Alessio
CS (1) Univ of Maryland, Baltimore, MD USA
SO Gastroenterology, (April, 2000) Vol. 118, No. 4 Suppl. 2 Part 1, pp. AGA A815. print..
Meeting Info.: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week. San Diego, California, USA May
21-24, 2000 American Gastroenterological Association
. ISSN: 0016-5085.
DT Conference
LA English
SL English
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Infection; Digestive System (Ingestion and Assimilation)
IT Chemicals & Biochemicals
zonulin
IT Miscellaneous Descriptors
gut barrier function; gut immune system; intestinal permeability; intracellular tight junction; small intestinal bacterial colonization; Meeting Abstract

L8 ANSWER 13 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS

AN 2000:257281 BIOSIS
DN PREV200000257281
TI Alterations in **Zonulin** secretion precedes the onset of diabetes in BB/Wor rats.
AU Watts, Tammara L. (1); Not, Tarcisio; Berti, Irene; Al Asmar, Ramzi; Di Pierro, Mariarosaria; Margaretten, Klara; Fasano, Alessio
CS (1) Univ of Maryland, Baltimore, MD USA
SO Gastroenterology, (April, 2000) Vol. 118, No. 4 Suppl. 2 Part 1, pp. AGA A603. print..
Meeting Info.: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week. San Diego, California, USA May
21-24, 2000 American Gastroenterological Association
. ISSN: 0016-5085.
DT Conference
LA English
SL English
IT Major Concepts
Endocrine System (Chemical Coordination and Homeostasis); Digestive System (Ingestion and Assimilation); Pharmacology
IT Diseases
diabetes: endocrine disease/pancreas, metabolic disease
IT Chemicals & Biochemicals
Zonulin: antidiabetic - drug
IT Alternate Indexing
Diabetes Mellitus (MeSH)
IT Miscellaneous Descriptors
intestinal permeability; Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
BB/Wor rat (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L8 ANSWER 14 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:508144 BIOSIS
DN PREV199900508144
TI Substantially pure **zonulin**, a physiological modulator of mammalian tight junctions.
AU Fasano, Alessio (1)
CS (1) Ellicott City, MD USA
ASSIGNEE: University of Maryland, Baltimore
PI US 5945510 Aug. 31, 1999
SO Official Gazette of the United States Patent and Trademark Office Patents,
(Aug. 31, 1999) Vol. 1225, No. 5, pp. NO PAGINATION.
ISSN: 0098-1133.
DT Patent
LA English
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology
IT Parts, Structures, & Systems of Organisms
tight junction
IT Chemicals & Biochemicals
zonulin: mammalian tight junction modulator

L8 ANSWER 15 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:331248 BIOSIS
DN PREV199900331248
TI Role of **zonulin** in the intestinal permeability changes typical of the acute phase of celiac disease.
AU Berti, Irene (1); Not, Tarcisio; Garofolo, Burlo; Fasano, Alessio (1)
CS (1) Univ of Maryland, Baltimore, MD USA
SO Gastroenterology, (April, 1999) Vol. 116, No. 4 PART 2, pp. A861. Meeting Info.: Digestive Disease Week and the 100th Annual Meeting of the American Gastroenterological Association Orlando, Florida, USA May 16-19, 1999 American Gastroenterological Association . ISSN: 0016-5085.
DT Conference
LA English
IT Major Concepts
Clinical Endocrinology (Human Medicine, Medical Sciences); Gastroenterology (Human Medicine, Medical Sciences)
IT Diseases
celiac disease: digestive system disease, metabolic disease
IT Chemicals & Biochemicals
anti-**zonulin** IgA antibody; **zonulin**
IT Alternate Indexing
Celiac Disease (MeSH)
IT Miscellaneous Descriptors
tight junction intestinal permeability; Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L8 ANSWER 16 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:223796 BIOSIS
DN PREV200100223796
TI Role of **zonulin** in the intestinal permeability changes typical of the acute phase of coeliac disease.
AU Not, T. (1); Berti, I.; Fasano, A.; Citta, A.; Ventura, A.
CS (1) Dept. of Pediatrics, Univ. of Maryland, Baltimore, MD USA
SO JPGN, (May, 1999) Vol. 28, No. 5, pp. 563. print.
Meeting Info.: 32nd Annual Meeting of the European Society of Pediatric Gastroenterology, Hepatology and Nutrition Warsaw, Poland June 02-05, 1999
ISSN: 0277-2116.
DT Conference
LA English
SL English
IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences); Gastroenterology (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
intestine: digestive system; serum: blood and lymphatics; small bowel: digestive system, histology; tight junction [tj]: digestive system, disassembly, intercellular, opening
IT Diseases
IDDM [insulin-dependent diabetes mellitus]: endocrine disease/pancreas,

immune system disease, metabolic disease; celiac disease: acute phase, diagnosis, digestive system disease, metabolic disease, pathogenesis; intestinal damage: digestive system disease; multiple sclerosis: immune system disease, nervous system disease

IT Chemicals & Biochemicals
IgA [immunoglobulin A]: serum level; IgG [immunoglobulin G]: serum level; anti-**zonulin** antibody: prevalence, serum level; gluten: dietary intake; **zonulin**: expression, hormone

IT Alternate Indexing
Celiac Disease (MeSH); Multiple Sclerosis (MeSH)

IT Methods & Equipment
ELISA [enzyme-linked immunosorbent assay]: detection/labeling techniques, diagnostic method; gluten-free diet: therapeutic method; in situ immunofluorescence test: diagnostic method; small bowel biopsy: diagnostic method

IT Miscellaneous Descriptors
intestinal permeability; Meeting Abstract

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): patient

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L8 ANSWER 17 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:288658 BIOSIS
DN PREV199800288658
TI Isolation and functional characterization of **zonulin**, a physiologic modulator of tight junctions.
AU Fasano, A.; Wang, W.; Nie, W.
CS Univ. Md., Baltimore, MD 21201 USA
SO Gastroenterology, (April 15, 1998) Vol. 114, No. 4 PART 2, pp. A1141. Meeting Info.: Digestive Diseases Week and the 99th Annual Meeting of the American Gastroenterological Association New Orleans, Louisiana, USA May 16-22, 1998 American Association for the Study of Liver Diseases . ISSN: 0016-5085.
DT Conference
LA English

IT Major Concepts
Biochemistry and Molecular Biophysics

IT Parts, Structures, & Systems of Organisms
tight junctions

IT Chemicals & Biochemicals
zonulin: functional characterization, isolation, zonula occludens toxin analogue

IT Miscellaneous Descriptors
Meeting Abstract

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): adult, fetus

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L10 ANSWER 1 OF 11 MEDLINE
AN 2001321408 MEDLINE
DN 21067442 PubMed ID: 11150657
TI Purification and preliminary characterization of the **zonula occludens toxin receptor** from human (CaCo2) and murine (IEC6) intestinal cell lines.
AU Uzzau S; Lu R; Wang W; Fiore C; Fasano A
CS Division of Pediatric Gastroenterology, Center for Vaccine Development, University of Maryland, School of Medicine, Baltimore, MD 21201, USA.. uzzau@ssmain.uniss.it
SO FEMS MICROBIOLOGY LETTERS, (2001 Jan 1) 194 (1) 1-5.
Journal code: FML; 7705721. ISSN: 0378-1097.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200106
ED Entered STN: 20010611
Last Updated on STN: 20010611
Entered PubMed: 20010126
Entered Medline: 20010607
AB In the present study, we report the preliminary characterization of the epithelial cell **receptor** for Vibrio cholerae **zonula occludens toxin** (Zot). Zot **receptor** was purified by ligand-affinity chromatography. Analysis of affinity-purified preparations by polyacrylamide gel electrophoresis revealed a protein of ca. 66 kDa. Partial N-terminal sequence obtained from purified murine and human Zot **receptor** revealed homology between the two proteins and with human alpha-1-chimaerin. Zot protein domain(s) involved in **receptor** binding were also analyzed by constructing several in frame deletion derivatives of a recombinant fusion Zot protein tagged with maltose binding protein. Our results suggest that Zot binding to its cellular membrane **receptor** requires a sequence that spans between amino acids 118 and 299.

L10 ANSWER 2 OF 11 MEDLINE
AN 2001100023 MEDLINE
DN 21035454 PubMed ID: 11193581
TI Stress-induced decrease of the intestinal barrier function. The role of muscarinic receptor activation.
AU Groot J; Bijlsma P; Van Kalkeren A; Kiliaan A; Saunders P; Perdue M
CS Institute for Neurobiology, University of Amsterdam, Amsterdam, The Netherlands.. groot@bio.uva.nl
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (2000) 915 237-46. Ref: 36
Journal code: 5NM. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals
EM 200102
ED Entered STN: 20010322
Last Updated on STN: 20010322

Entered PubMed: 20010118
Entered Medline: 20010201
AB Recently the breakdown of the barrier function of the intestinal epithelium after application of an experimental psychological and physical stress protocol in rats has been observed. Not only did smaller molecules pass from the luminal to the serosal side, but so also did larger proteins with the dimensions of luminal antigens and **toxins**. The increased permeability for macromolecules is primarily due to a decrease of the tightness of the **zonula occludens**, but an increased endocytotic uptake indicates that transcytosis is increased also. From studies of model systems it can be concluded that activation of the intracellular protein kinase C route by muscarinic **receptor** activation or histamine **receptor** activation can be one of the underlying cellular pathways. The physical pathway relaying the stress from the brain to the intestinal tract appears to be the parasympathetic branch of the autonomic nervous system. The difference in reaction of different strains suggests that coping style is an important determinant of the response of the intestinal barrier to stress.

L10 ANSWER 3 OF 11 MEDLINE
AN 97457190 MEDLINE
DN 97457190 PubMed ID: 9311128
TI Characterization of filamentous phages of Vibrio cholerae O139 and O1.
AU Ehara M; Shimodori S; Kojima F; Ichinose Y; Hirayama T; Albert M J; Supawat K; Honma Y; Iwanaga M; Amako K
CS Department of Bacteriology, Nagasaki University, Japan.. ehara@net.nagasaki-u.ac.jp
SO FEMS MICROBIOLOGY LETTERS, (1997 Sep 15) 154 (2) 293-301. Journal code: FML; 7705721. ISSN: 0378-1097.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-D89074
EM 199710
ED Entered STN: 19971024
Last Updated on STN: 19971024
Entered Medline: 19971016
AB We have analyzed our collection of Vibrio cholerae O139 strains to determine whether filamentous phages are produced in their culture supernatants, and whether any replicative form of DNA is detectable in cell lysates. Two types of filamentous phage, designated fs1 (6.4 kb) and fs2 (8.5 kb), were found in strains of Vibrio cholerae O139, fs1 was commonly produced from clinical isolates of Vibrio cholerae O1. Infectious particles (filamentous phages) were inducible by subculture, mitomycin C, and cultivation in a ligated ileal loop of a rabbit. Type 4 fimbriae of Vibrio cholerae O1 sensitive to D-glucose and D-mannose were suggested to be **receptors** for fs1 and fs2. The genome of fs1 was revealed to encode a potential new enterotoxin homologous to **zonula occludens toxin**. Clarification of the relation of type 4 fimbriae and these filamentous phages will provide a new understanding of the colonization of Vibrio-cholerae O1 and O139. Thus the presence of a new enterotoxin encoded by the genome of filamentous phage like fs1 may

clarify the pathogenesis of cholera **toxin** negative clinical isolates of Vibrio cholerae O1 and non-O1. Our findings combined with the earlier report by Ehara et al. [Microbio. Immunol. 37 (1993) 679-688] suggest that type 4 fimbriae of Vibrio cholerae O1 are important for the development of an effective vaccine against cholera.

L10 ANSWER 4 OF 11 MEDLINE
AN 97193660 MEDLINE
DN 97193660 PubMed ID: 9041245
TI The enterotoxic effect of zonula occludens toxin on rabbit small intestine
involves the paracellular pathway.
AU Fasano A; Uzzau S; Fiore C; Margaretten K
CS Division of Pediatric Gastroenterology and Nutrition, Center for Vaccine Development, University of Maryland School of Medicine, Baltimore, USA.
NC AI-35740 (NIAID)
DK-48373 (NIDDK)
SO GASTROENTEROLOGY, (1997 Mar) 112 (3) 839-46.
Journal code: FH3; 0374630. ISSN: 0016-5085.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199703
ED Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970320
AB BACKGROUND & AIMS: **Zonula occludens toxin** is a novel **toxin** elaborated by Vibrio cholerae that modulates intestinal tight junctions. The aim of this study was to establish whether the permeabilizing effect of the **toxin** leads to intestinal secretion. METHODS: Rabbit intestine was mounted in Ussing chambers and exposed to increasing concentrations of purified **toxin**. The tissues were also fixed, exposed to **zonula occludens toxin**, and processed for fluorescence microscopy to determine the distribution of the **toxin receptor** within the intestine. Then purified **toxin** was simultaneously perfused in three distinct rabbit intestinal segments in vivo, and water and electrolyte absorption were measured. RESULTS: **Zonula occludens toxin** induced a time- and dose-dependent decrease of tissue resistance starting at a **toxin** concentration of 1.1 x 10(-13) mol/L. When tested in vivo, the **toxin** induced a secretion of water and chloride and the passage of polyethylene glycol 4000 in the bloodstream. Both the in vitro and in vivo effects of the **toxin** were observed only in the small intestine but not in the colon and paralleled the distribution of the **toxin receptor** within the intestine. CONCLUSIONS: The intestinal secretion induced by **zonula occludens toxin** follows the opening of tight junctions caused by the **toxin**, possibly representing a novel mechanism of intestinal secretion.

L10 ANSWER 5 OF 11 MEDLINE
AN 95362830 MEDLINE
DN 95362830 PubMed ID: 7635964
TI **Zonula occludens toxin** modulates tight junctions through protein kinase C-dependent actin reorganization, in

vitro.
AU Fasano A; Fiorentini C; Donelli G; Uzzau S; Kaper J B; Margaretten K; Ding
X; Guandalini S; Comstock L; Goldblum S E
CS Division of Pediatric Gastroenterology and Nutrition, University of Maryland School of Medicine, Baltimore 21201, USA.
NC AI19716 (NIAID)
SO JOURNAL OF CLINICAL INVESTIGATION, (1995 Aug) 96 (2) 710-20.
Journal code: HS7; 7802877. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199509
ED Entered STN: 19950921
Last Updated on STN: 19950921
Entered Medline: 19950911
AB The intracellular signaling involved in the mechanism of action of **zonula occludens toxin** (ZOT) was studied using several in vitro and ex vivo models. ZOT showed a selective effect among various cell lines tested, suggesting that it may interact with a specific **receptor**, whose surface expression on various cells differs. When tested in IEC6 cell monolayers, ZOT-containing supernatants induced a redistribution of the F-actin cytoskeleton. Similar results were obtained with rabbit ileal mucosa, where the reorganization of F-actin paralleled the increase in tissue permeability. In endothelial cells, the cytoskeletal rearrangement involved a decrease of the soluble G-actin pool (-27%) and a reciprocal increase in the filamentous F-actin pool (+22%). This actin polymerization was time- and dose-dependent, and was reversible. Pretreatment with a specific protein kinase C inhibitor, CGP41251, completely abolished the ZOT effects on both tissue permeability and actin polymerization. In IEC6 cells ZOT induced a peak increment of the PKC-alpha isoform after 3 min incubation. Taken together, these results suggest that ZOT activates a complex intracellular cascade of events that regulate tight junction permeability, probably mimicking the effect of physiologic modulator(s) of epithelial barrier function.

L10 ANSWER 6 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:265873 BIOSIS
DN PREV200000265873
TI **Zonula occludens toxin** (Zot) structure-function analysis: Identification of active fragment and the **receptor** binding domain.
AU Fasano, Alessio (1); Di Pierro, Mariarosaria; Lu, Ruliang; Uzzau, Sergio; Wang, Wenle; Margaretten, Klara; Maimone, Francesco
CS (1) Universita' degli Study di Bari, Bari Italy
SO Gastroenterology, (April, 2000) Vol. 118, No. 4 Suppl. 2 Part 1, pp. AGA A814. print..
Meeting Info.: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week. San Diego, California, USA May 21-24, 2000 American Gastroenterological Association
. ISSN: 0016-5085.
DT Conference

LA English
SL English
IT Major Concepts
Biochemistry and Molecular Biophysics; Digestive System (Ingestion and Assimilation)
IT Chemicals & Biochemicals
C-terminus cleavage product; **Zonula occludens toxin**: active fragment, enterotoxin, function, **receptor** binding domain, structure
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Vibrionaceae: Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms
ORGN Organism Name
Vibrio cholerae (Vibrionaceae): pathogen
ORGN Organism Superterms
Bacteria; Eubacteria; Microorganisms

L10 ANSWER 7 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:508171 BIOSIS
DN PREV199900508171
TI Zonula occludens toxic receptor.
AU Fasano, Alessio (1)
CS (1) Ellicott City, MD USA
ASSIGNEE: University of Maryland at Baltimore
PI US 5948629 Sep. 07, 1999
SO Official Gazette of the United States Patent and Trademark Office Patents,
(Sep. 7, 1999) Vol. 1226, No. 1, pp. NO PAGINATION.
ISSN: 0098-1133.
DT Patent
LA English
IT Major Concepts
Biochemistry and Molecular Biophysics; Toxicology
IT Chemicals & Biochemicals
zonula occludens toxin: receptor , toxin
ORGN Super Taxa
Vibrionaceae: Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms
ORGN Organism Name
Vibrio cholera (Vibrionaceae)
ORGN Organism Superterms
Bacteria; Eubacteria; Microorganisms

L10 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:392983 BIOSIS
DN PREV199900392983
TI **Zonula occludens toxin receptors.**
AU Fasano, Alessio (1)
CS (1) Ellicott City, MD USA
ASSIGNEE: University of Maryland, Baltimore
PI US 5912323 Jun. 15, 1999
SO Official Gazette of the United States Patent and Trademark Office Patents,
(Jun.15, 1999) Vol. 1223, No. 3, pp. NO PAGINATION.

ISSN: 0098-1133.
DT Patent
LA English
IT Major Concepts
Bioprocess Engineering; Pharmacology; Toxicology
IT Chemicals & Biochemicals
zonula occludens toxin: toxin
IT Miscellaneous Descriptors
zonula occludens toxin receptors
ORGN Super Taxa
Vibrionaceae: Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms
ORGN Organism Name
Vibrio cholera (Vibrionaceae)
ORGN Organism Superterms
Bacteria; Eubacteria; Microorganisms

L10 ANSWER 9 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:97412 BIOSIS
DN PREV199900097412
TI **Zonula occludens toxin receptor.**
AU Fasano, A.
CS Ellicott City, Md. USA
ASSIGNEE: UNIVERSITY OF MARYLAND AT BALTIMORE
PI US 5864014 Jan. 26, 1999
SO Official Gazette of the United States Patent and Trademark Office Patents,
(Jan. 26, 1999) Vol. 1218, No. 4, pp. 3159.
ISSN: 0098-1133.
DT Patent
LA English
IT Major Concepts
Biochemistry and Molecular Biophysics; Bioprocess Engineering; Infection; Toxicology
IT Sequence Data
AMINO ACID SEQUENCE
IT Miscellaneous Descriptors
BACTERIA; BIOTECHNOLOGY; MOLECULAR SEQUENCE DATA; MOLECULAR WEIGHT; **ZONULA OCCLUDENS TOXIN RECEPTOR**
ORGN Super Taxa
Vibrionaceae: Eubacteria, Bacteria
ORGN Organism Name
microorganism (Microorganisms - Unspecified); Vibrio cholera (Vibrionaceae)
ORGN Organism Superterms
bacteria; eubacteria; microorganisms

L10 ANSWER 10 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:288737 BIOSIS
DN PREV199800288737
TI Purification of the **zonula occludens toxin** (ZOT) human **receptor.**
AU Lu, R.; Vigorito, R.; Wisniewski, S.; Zielke, H. R.; Wang, W.; Fasano, A.
CS Univ. Maryland, Baltimore, MD 21201 USA
SO Gastroenterology, (April 15, 1998) Vol. 114, No. 4 PART 2, pp. A1160-A1161.
Meeting Info.: Digestive Diseases Week and the 99th Annual Meeting of the

American Gastroenterological Association New Orleans, Louisiana, USA May 16-22, 1998 American Association for the Study of Liver Diseases . ISSN: 0016-5085.
DT Conference
LA English
IT Major Concepts
Membranes (Cell Biology)
IT Parts, Structures, & Systems of Organisms
zonula occludens toxin receptor
: purification
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
CaCo-2 (Hominidae); T84 (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L10 ANSWER 11 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1996:298158 BIOSIS
DN PREV199699020514
TI Distribution and nature of **zonula occludens toxin** (ZOT) **receptor** in eukaryotic cells.
AU Fiore, Cara R.; Uzzau, Sergio; Fasano, Alessio
CS Gastrointestinal Pathophysiol. Unit, Cent. Vaccine Dev., Univ. Maryland Sch. Med., Baltimore, MD 21201 USA
SO Gastroenterology, (1996) Vol. 110, No. 4 SUPPL., pp. A323.
Meeting Info.: 96th Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week San Francisco, California, USA May 19-22, 1996
ISSN: 0016-5085.
DT Conference
LA English
IT Major Concepts
Gastroenterology (Human Medicine, Medical Sciences); Infection; Membranes (Cell Biology); Physiology; Toxicology
IT Miscellaneous Descriptors
INTESTINAL PERMEABILITY; MEETING ABSTRACT
ORGN Super Taxa
Bovidae: Artiodactyla, Mammalia, Vertebrata, Chordata, Animalia; Canidae: Carnivora, Mammalia, Vertebrata, Chordata, Animalia; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Leporidae: Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia; Vibrionaceae: Eubacteria, Bacteria
ORGN Organism Name
bovine (Bovidae); dog (Canidae); human (Hominidae); rabbit (Leporidae);
Vibrio cholerae (Vibrionaceae)
ORGN Organism Superterms
animals; artiodactyls; bacteria; carnivores; chordates; eubacteria; humans; lagomorphs; mammals; microorganisms; nonhuman mammals; nonhuman
vertebrates; primates; vertebrates